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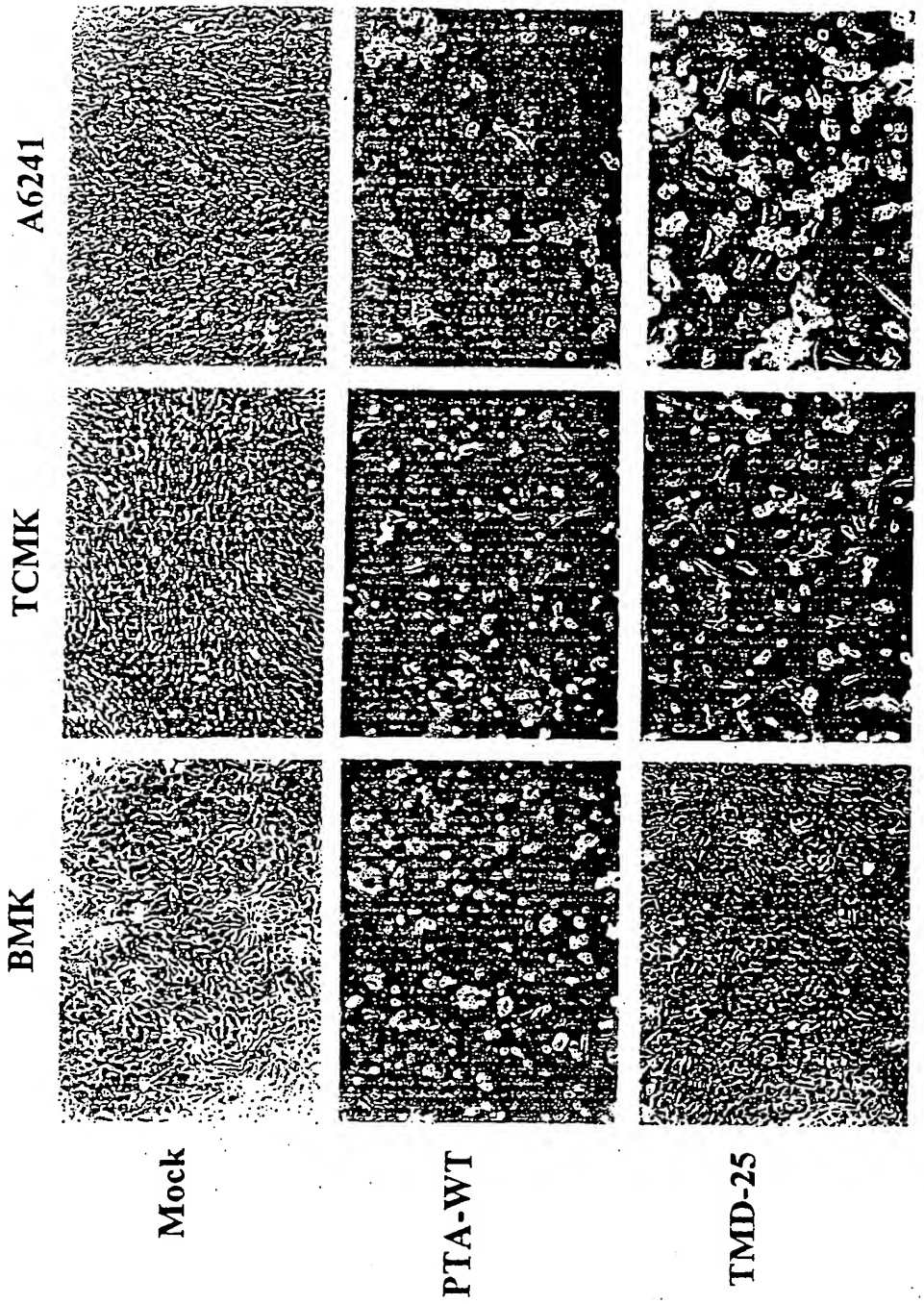
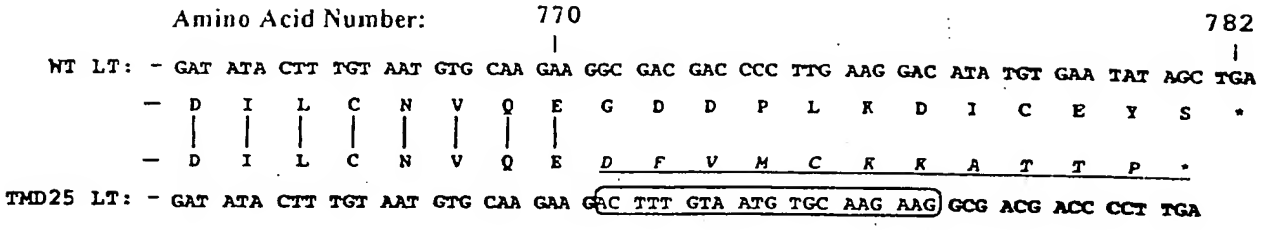
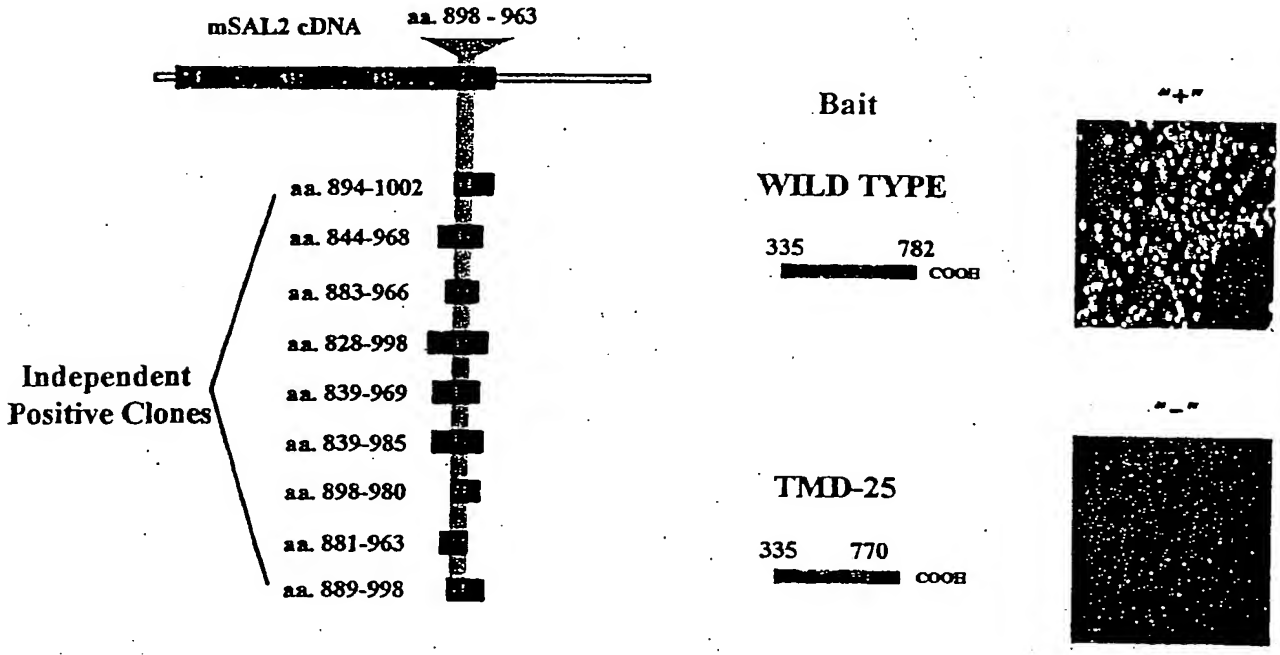


Fig. 1

A



B.

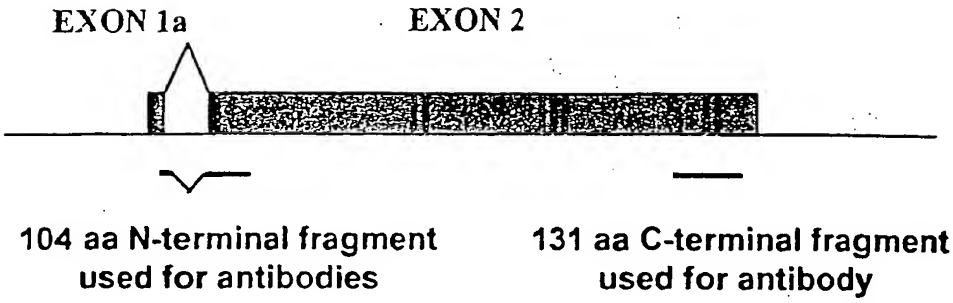


C.

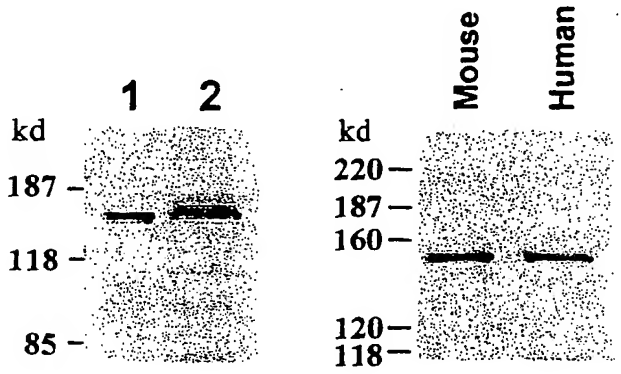
Large T Deletions																		Growth on His⁻ Plate
Wild Type	—	N	V	Q	E	G	D	D	P	L	K	D	I	C	E	Y	S	*	+
335-780	—	N	V	Q	E	G	D	D	P	L	K	D	I	C	E	*			+
335-776	—	N	V	Q	E	G	D	D	P	L	K	*							+
335-774	—	N	V	Q	E	G	D	D	*										–
335-770	—	N	V	Q	E	*													–
Δ 774	—	N	V	Q	E	G	D	D	_	L	K	D	I	C	E	Y	S	*	+
Δ 775	—	N	V	Q	E	G	D	D	P	_	K	D	I	C	E	Y	S	*	+
Δ 776	—	N	V	Q	E	G	D	D	P	L	_	D	I	C	E	Y	S	*	+
Δ 774-776	—	N	V	Q	E	G	D	D	_	_	_	D	I	C	E	Y	S	*	–

Fig. 2

A.


EXON 1a
EXON 2
104 aa N-terminal fragment used for antibodies
131 aa C-terminal fragment used for antibody

B.


1
2
kd
187
118
85
Mouse
Human
kd
220
187
160
120
118

C.

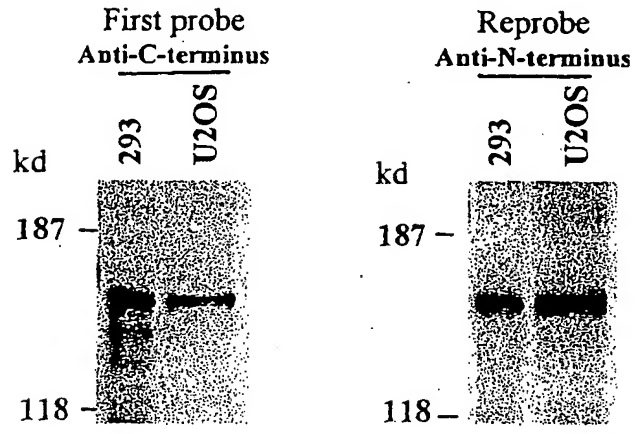
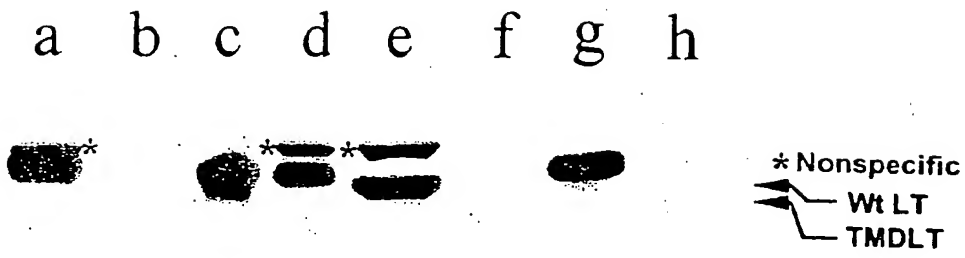

First probe
Anti-C-terminus
293
U2OS
kd
187
118
Reprobe
Anti-N-terminus
293
U2OS
kd
187
118

Fig. 3

A.


a b c d e f g h
* Nonspecific
Wt LT
TMDLT

B.

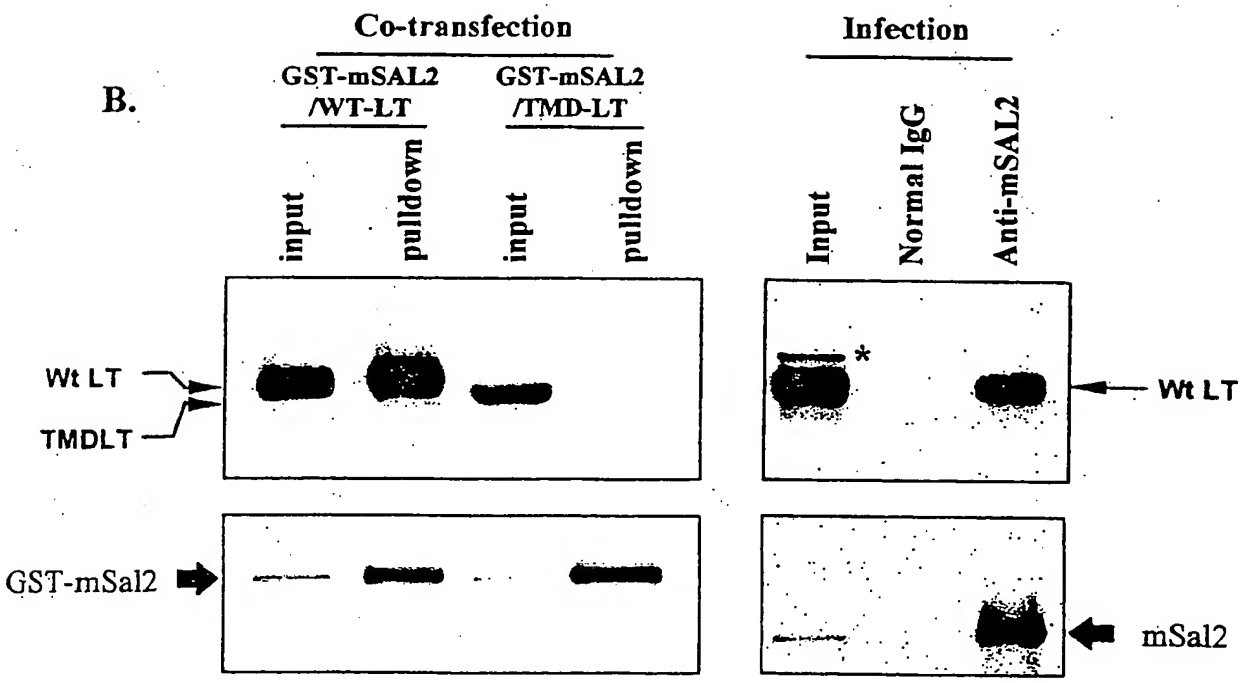
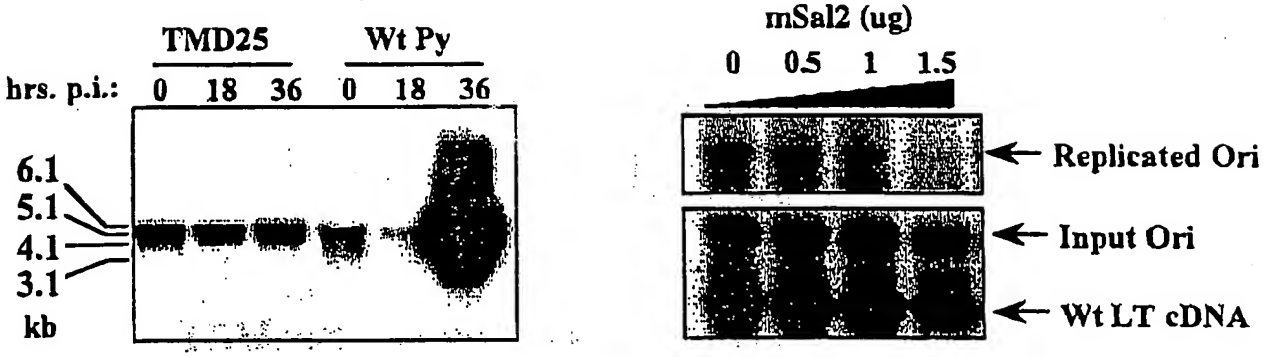

Co-transfection
Infection
GST-mSAL2 /WT-LT
GST-mSAL2 /TMD-LT
input
pulldown
input
pulldown
Input
Normal IgG
Anti-mSAL2
Wt LT
TMDLT
Wt LT
GST-mSal2
mSal2

Fig. 4

A

TMD-25 WILD TYPE

B



C

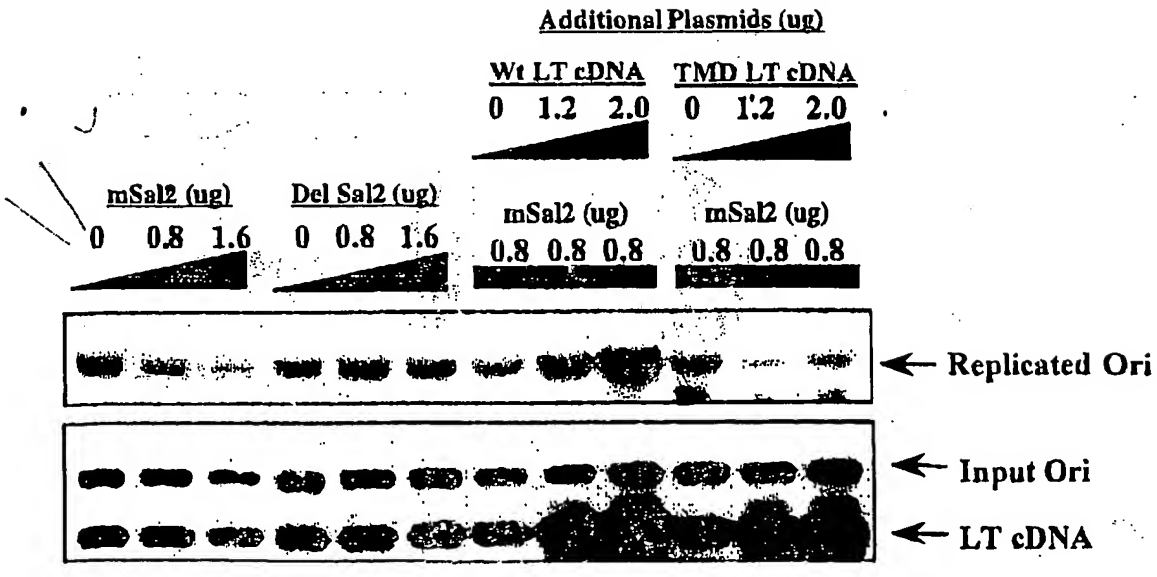


Figure 5

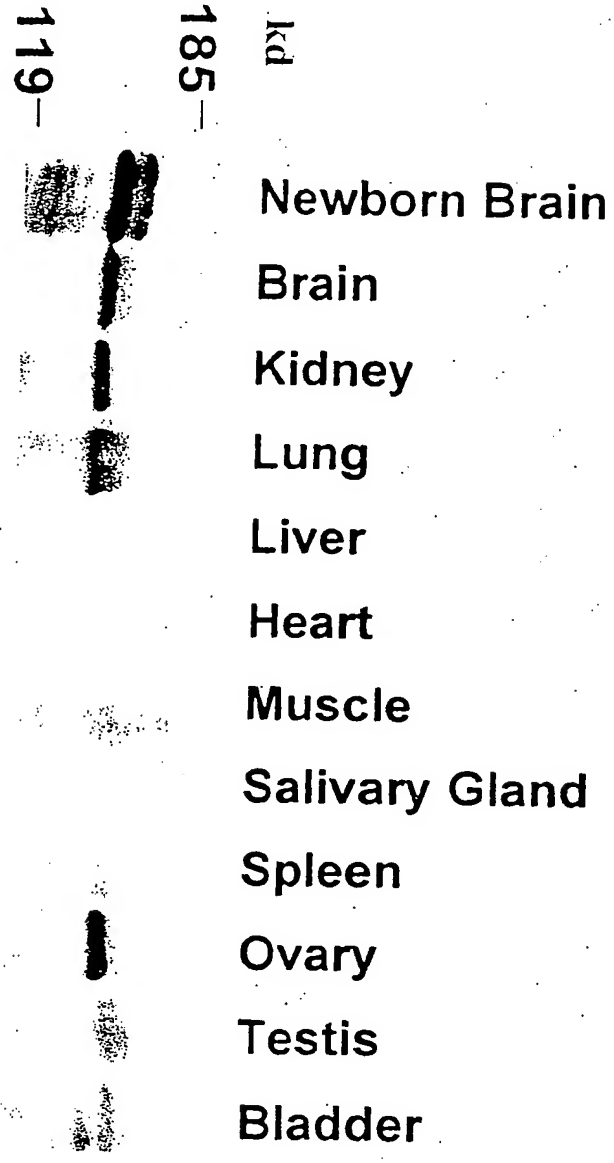

kd
185
119
Newborn Brain
Brain
Kidney
Lung
Liver
Heart
Muscle
Salivary Gland
Spleen
Ovary
Testis
Bladder

Fig. 6

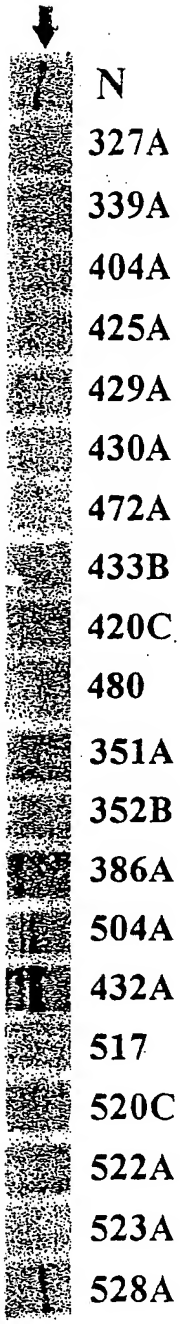

N
327A
339A
404A
425A
429A
430A
472A
433B
420C
480
351A
352B
386A
504A
432A
517
520C
522A
523A
528A

Fig. 7

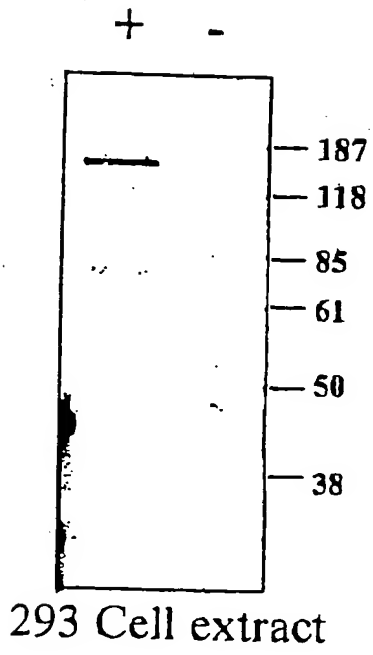
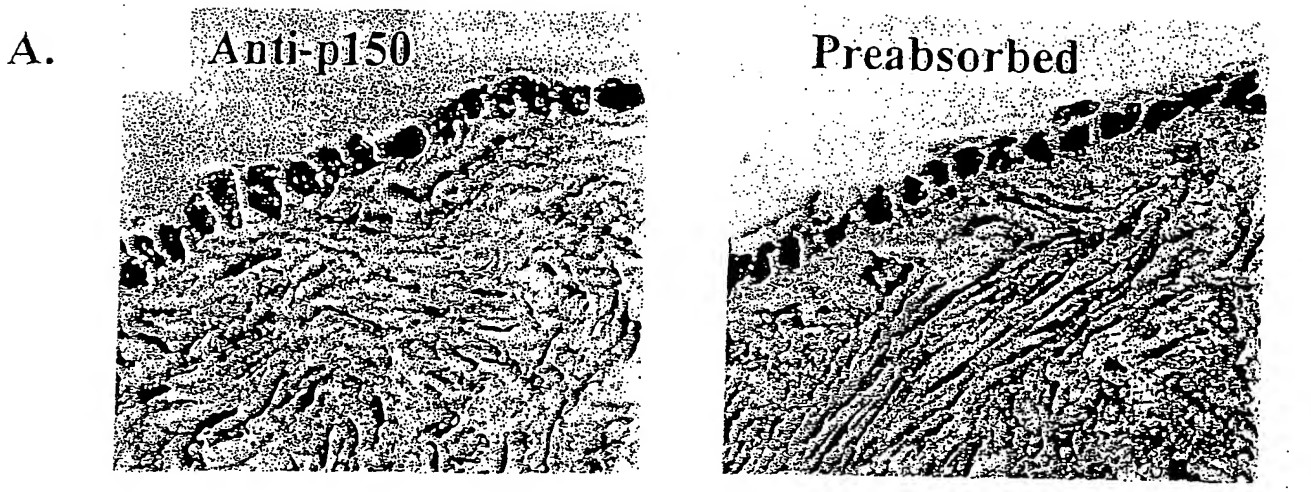


Fig. 8


A.
Anti-p150
Preabsorbed

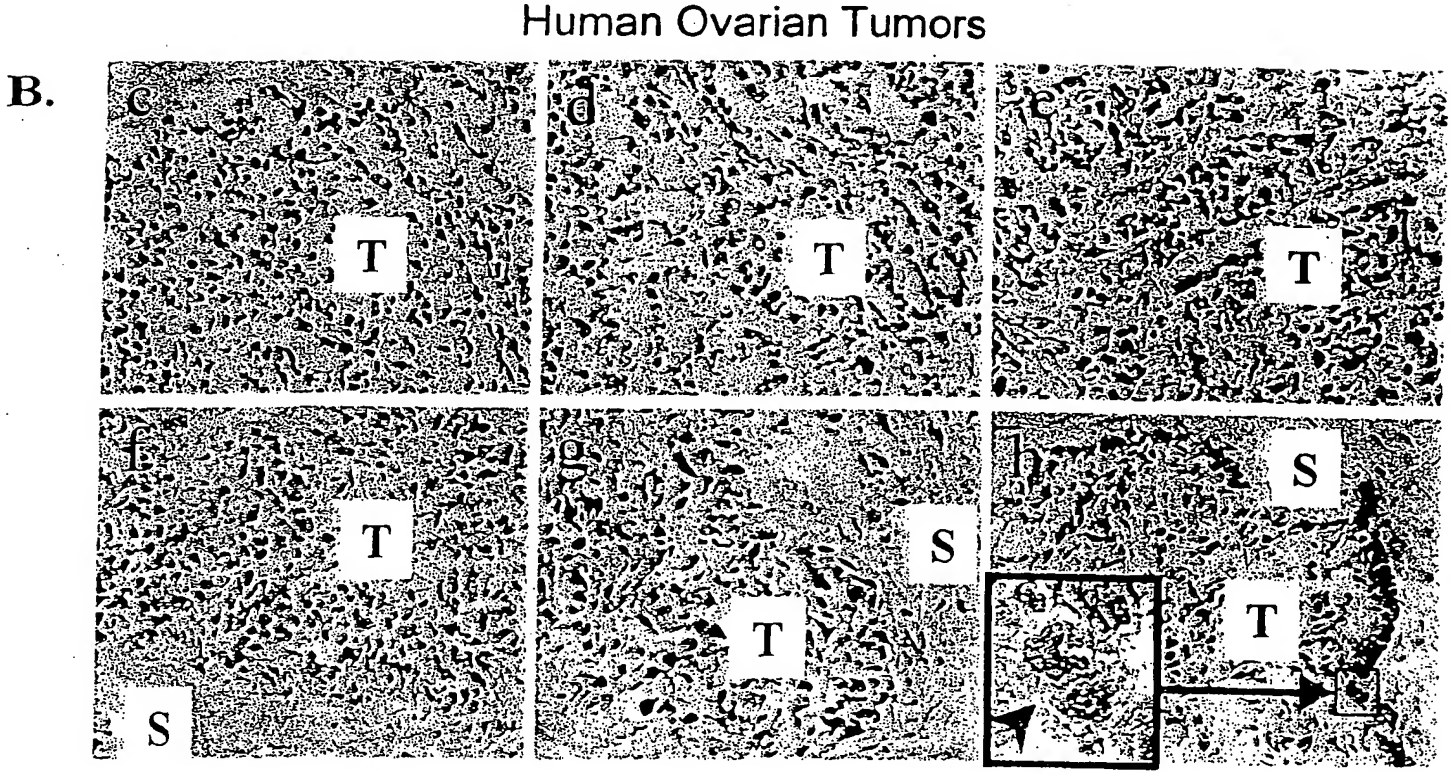
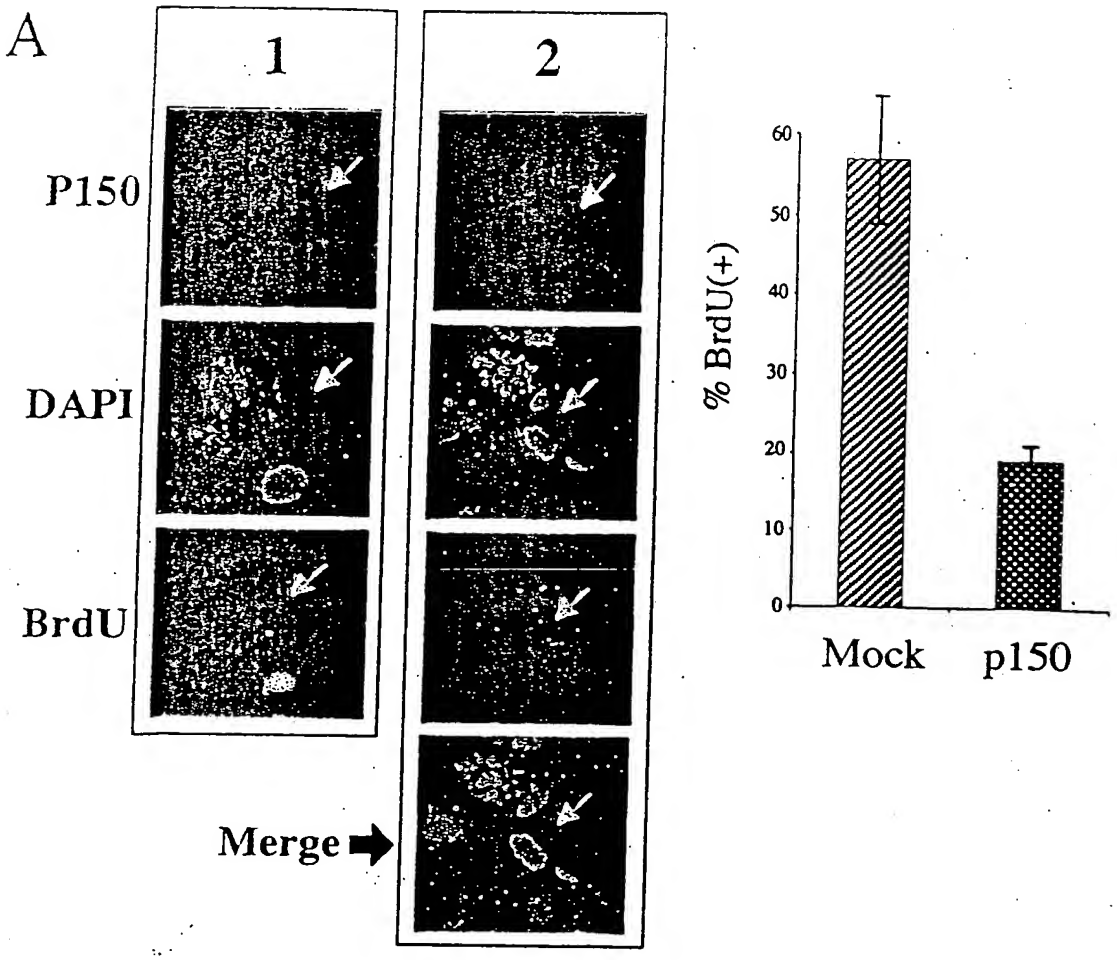

Human Ovarian Tumors
B.
c
T
d
T
e
T
f
T
S
g
S
T
h
S
T

Fig. 9


A
1
2
P150
DAPI
BrdU
Merge
% BrdU(+)
60
50
40
30
20
10
0
Mock
p150

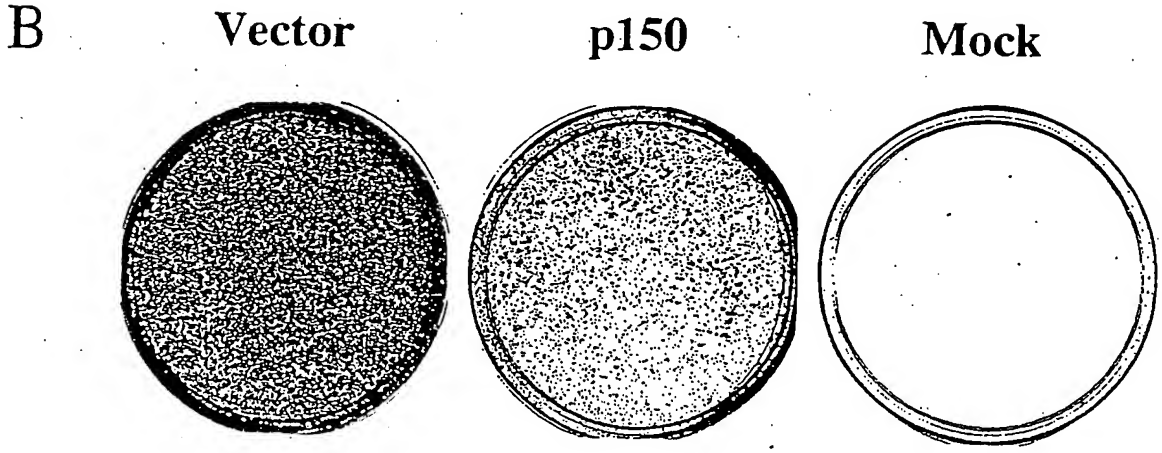

B
Vector
p150
Mock

Fig. 10

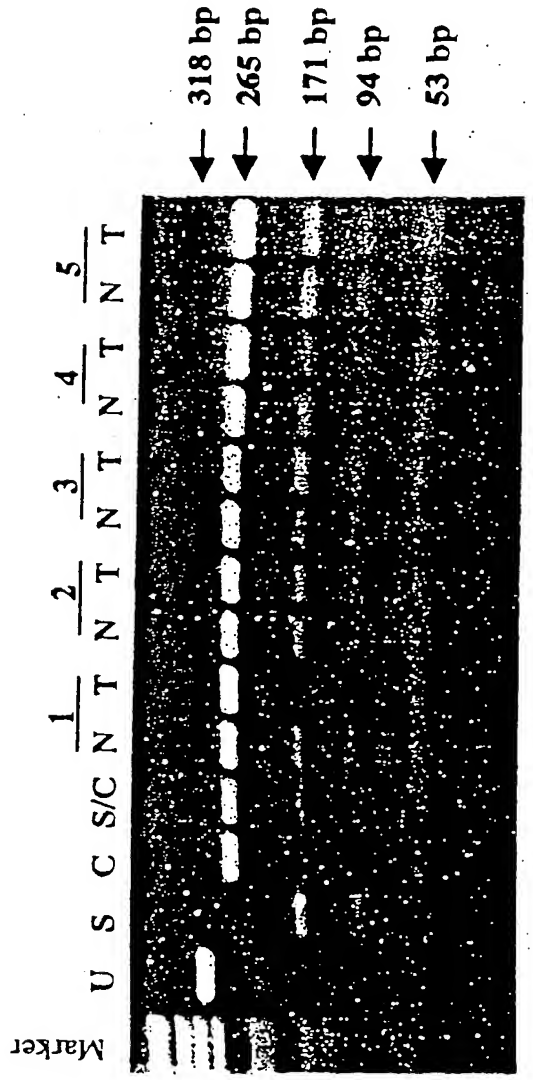


Fig. 11

FIG. 12

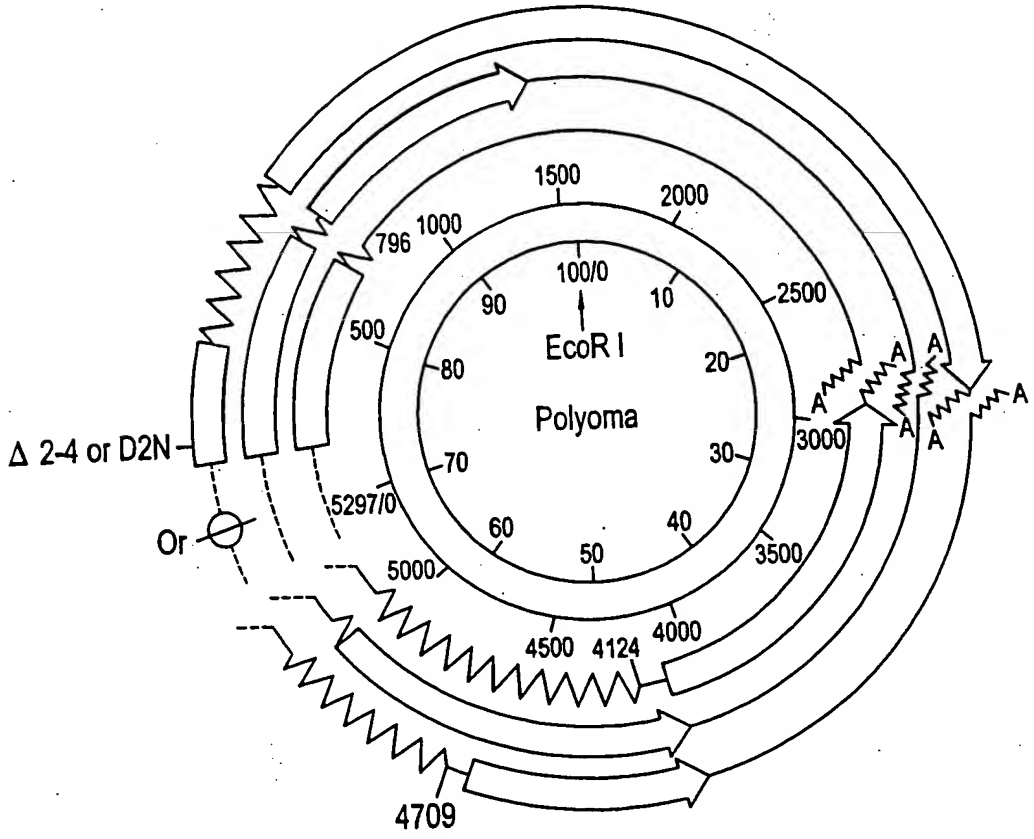

1500
2000
1000
796
100/0
90
10
2500
500
EcoR I
80
20
Polyoma
70
30
3000
5297/0
60
40
50
3500
5000
4500
4124
4000
4709
Δ 2-4 or D2N
Or
A
A
A
A
A
A

FIG. 13

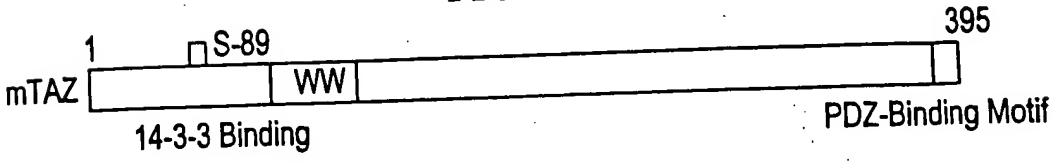

1
S-89
395
mTAZ
WW
14-3-3 Binding
PDZ-Binding Motif

FIG. 14

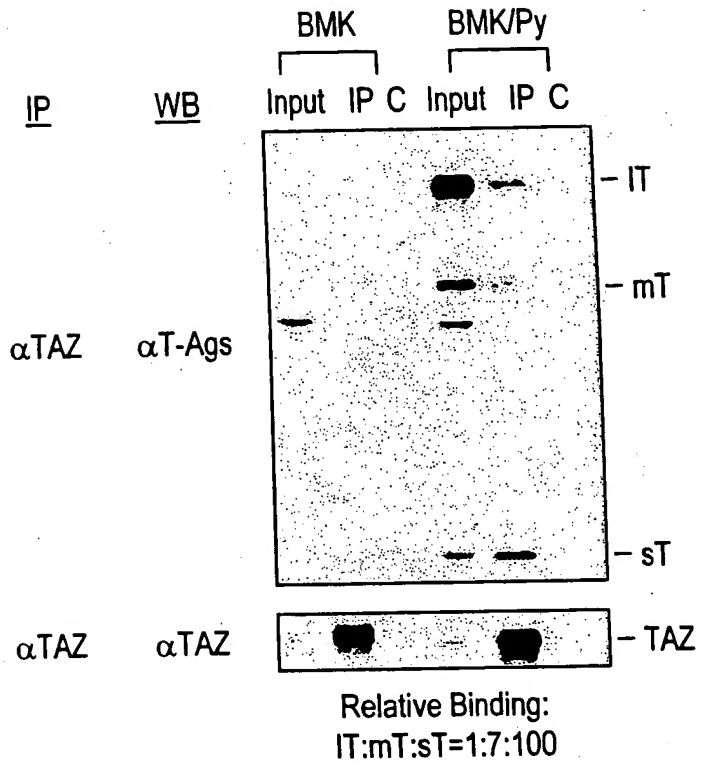

BMK
BMK/Py
IP
WB
Input IP C Input IP C
– IT
– mT
αTAZ
αT-Ags
– sT
αTAZ
αTAZ
– TAZ
Relative Binding:
IT:mT:sT=1:7:100

FIG. 15

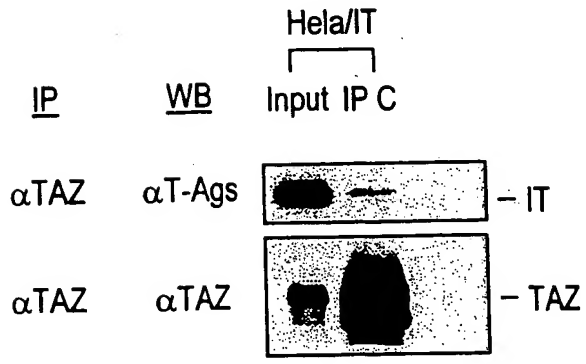

Hela/IT
IP
WB
Input IP C
αTAZ
αT-Ags
– IT
αTAZ
αTAZ
– TAZ

FIG. 16A

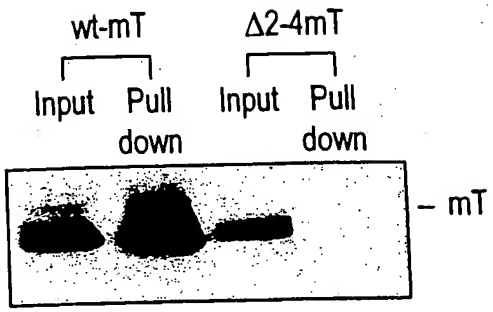


FIG. 16B

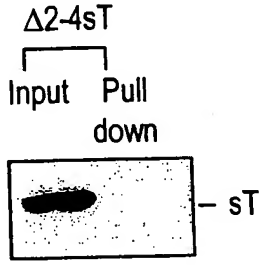


FIG. 17

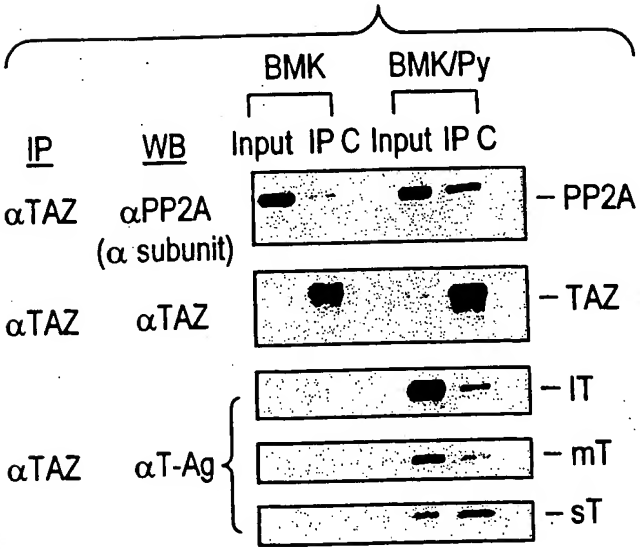


FIG. 18

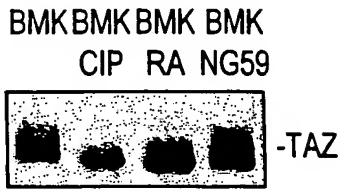


FIG. 19

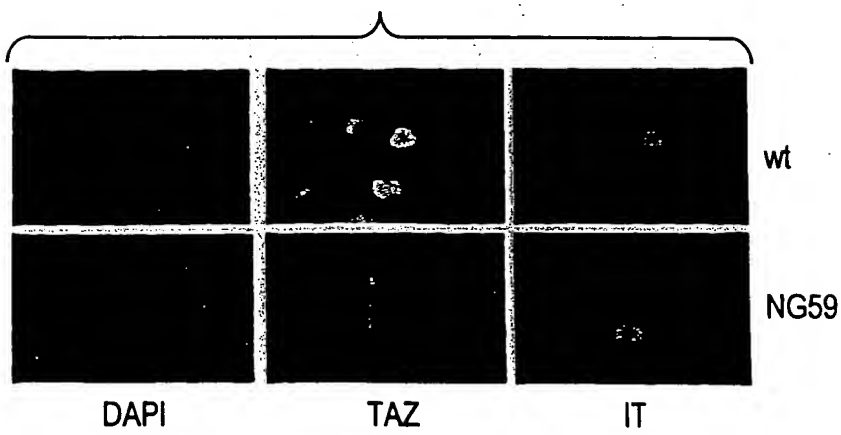


FIG. 20

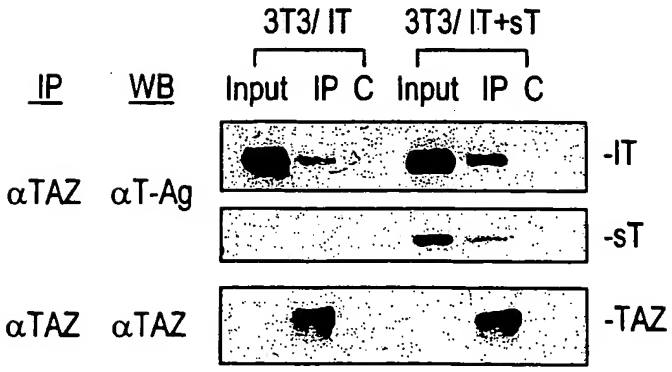


FIG. 21

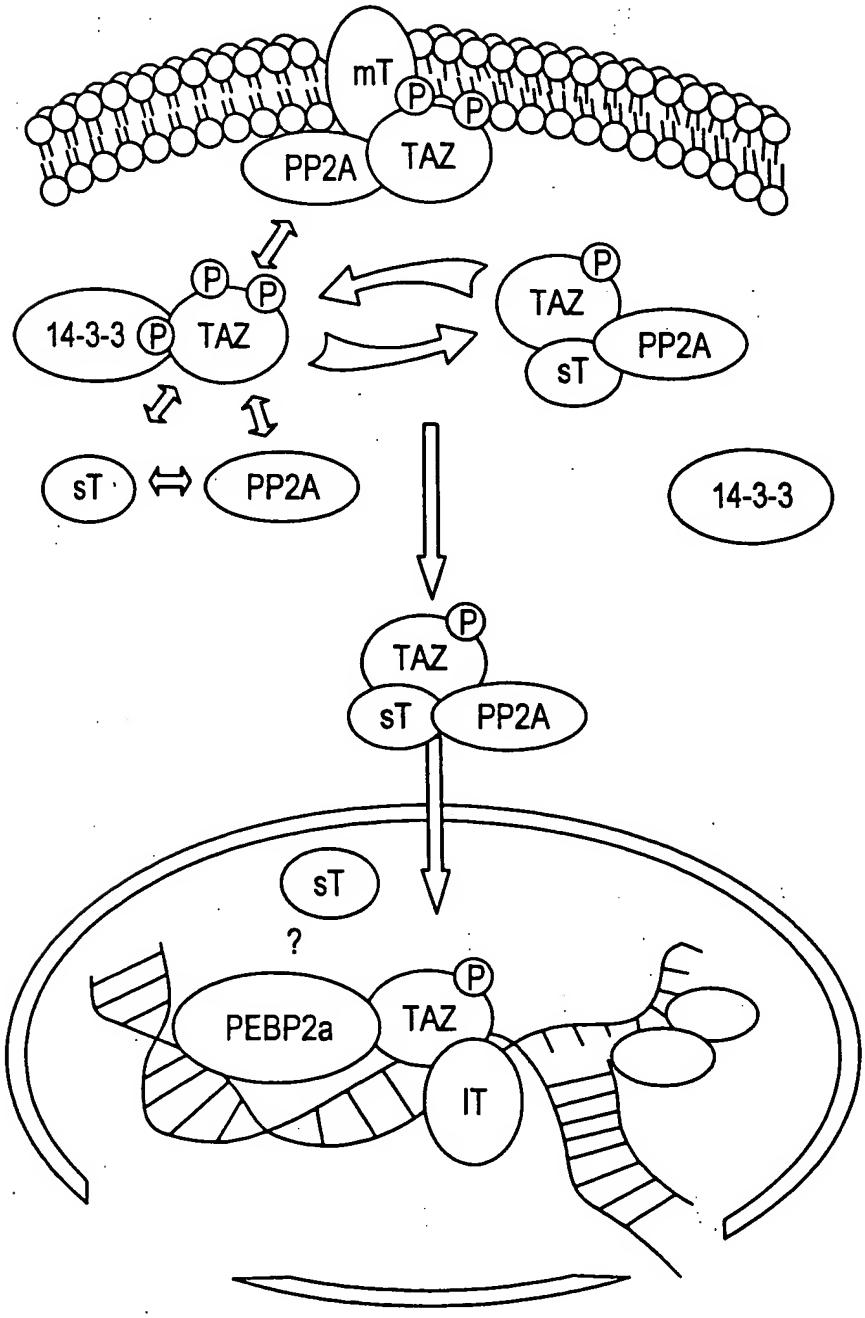

mT
P
P
PP2A
TAZ
P
P
14-3-3
P
TAZ
P
TAZ
sT
PP2A
sT
PP2A
14-3-3
P
TAZ
sT
PP2A
sT
?
PEBP2a
P
TAZ
IT

FIG. 22A

```
GGGGGGTTTGAAATGGCTTCTCGGTTAACCCGGGCCAGACTCAGGTATCTGCTATAGAAGGGAAACAAGTGAAAGTTTTCCCCCCCTTGCATCATGGCTCAGT  103
CCCCCCAAACTTTACCGAAGAGCCAATTGGGCCCGGTCTGAGTCCATAGACGATATCTTCCCTTTGTTCACTTTCAAAAGGGGGGGAACGTAGTACCGAGTCA
 G  G  F  E  M  A  S  R  L  T  R  A  R  L  R  Y  L  L  .  K  G  N  K  .  K  F  S  P  P  C  I  M  A  Q

TTGGAGGACAGAAGAATCCACCATGGGCTACTCAGTTTACAGCCACTGCGGTCTCACAACCAGCTGCACTAGGTGTTCAGCAGCCATCACTTCTGGGAGCATC  206
AACCTCCTGTCTTCTTAGGTGGTACCCGATGAGTCAAATGTCGGTGACGCCAGAGTGTTGGTCGACGTGATCCACAAGTCGTCGGTAGTGAAGACCCTCGTAG
 F  G  G  Q  K  N  P  P  W  A  T  Q  F  T  A  T  A  V  S  Q  P  A  A  L  G  V  Q  Q  P  S  L  L  G  A  S

TCCTACCATTTATACCCAGCAGACTGCATTGGCGGCGGCAGGCCTTACCACACAAACGCCAGCAAACTATCAGTTAACACAAACTGCGGCACTGCAGCAACAA  309
AGGATGGTAAATATGGGTCGTCTGACGTAACCGCCGCCGTCCGGAATGGTGTGTTTGCGGTCGTTTGATAGTCAATTGTGTTTGACGCCGTGACGTCGTTGTT
  P  T  I  Y  T  Q  Q  T  A  L  A  A  A  G  L  T  T  Q  T  P  A  N  Y  Q  L  T  Q  T  A  A  L  Q  Q  Q

GCTGCAGCTGTATTACAGCAGCAATATTCACAACCTCAGCAGGCCTTGTATAGTGTGCAGCAGCAGTTGCAACAACCTCAGCAGACCATTTTAACACAGCCAG  412
CGACGTCGACATAATGTCGTCGTTATAAGTGTTGGAGTCGTCCGGAACATATCACACGTCGTCGTCAACGTTGTTGGAGTCGTCTGGTAAAATTGTGTCGGTC
 A  A  A  V  L  Q  Q  Q  Y  S  Q  P  Q  Q  A  L  Y  S  V  Q  Q  Q  L  Q  Q  P  Q  Q  T  I  L  T  Q  P

CTGTTGCATTGCCCACAAGCCTTAGCCTGTCGACTCCTCAGCCTGCAGCACAGATTACTGTATCATATCCAACACCAAGGTCCAGTCAACAGCAAACTCAACC  515
GACAACGTAACGGGTGTTCGGAATCGGACAGCTGAGGAGTCGGACGTCGTGTCTAATGACATAGTATAGGTTGTGGTTCCAGGTCAGTTGTCGTTTGAGTTGG
 A  V  A  L  P  T  S  L  S  L  S  T  P  Q  P  A  A  Q  I  T  V  S  Y  P  T  P  R  S  S  Q  Q  Q  T  Q  P

TCAGAAGCAGCGTGTTTTCACAGGAGTGGTTACAAAGCTACATGATACATTTGGATTTGTGGATGAAGATGTATTCTTTCAGCTTGGTGCTGTTAAAGGGAAA  618
AGTCTTCGTCGCACAAAAGTGTCCTCACCAATGTTTCGATGTACTATGTAAACCTAAACACCTACTTCTACATAAGAAAGTCGAACCACGACAATTTCCCTTT
  Q  K  Q  R  V  F  T  G  V  V  T  K  L  H  D  T  F  G  F  V  D  E  D  V  F  F  Q  L  G  A  V  K  G  K

ACCCCCCAAGTTGGTGATAGAGTATTGGTTGAAGCAACTTATAATCCTAATATGCCTTTTAAATGGAATGCACAAAGAATTCAAACACTACCAAATCAGAATC  721
TGGGGGGTTCAACCACTATCTCATAACCAACTTCGTTGAATATTAGGATTATACGGAAAATTTACCTTACGTGTTTCTTAAGTTTGTGATGGTTTAGTCTTAG
 T  P  Q  V  G  D  R  V  L  V  E  A  T  Y  N  P  N  M  P  F  K  W  N  A  Q  R  I  Q  T  L  P  N  Q  N

AGTCTCAAACGCAACCTTTACTGAAGACTCCGACTGCTGTTATTCAGCCGATTGTGCCACAGACAACGTTTGGTGTTCAGGCACAGCCCCAACCCCAGTCATT  824
TCAGAGTTTGCGTTGGAAATGACTTCTGAGGCTGACGACAATAAGTCGGCTAACACGGTGTCTGTTGCAAACCACAAGTCCGTGTCGGGGTTGGGGTCAGTAA
 Q  S  Q  T  Q  P  L  L  K  T  P  T  A  V  I  Q  P  I  V  P  Q  T  T  F  G  V  Q  A  Q  P  Q  P  Q  S  L
```

FIG. 22B

```
ATTGCAGGCCCAGATCTCAGCTGCCTCTATTACACCACTATTGCAGACGCAGCCACAGCCCTTATTACAGCAGCCACAGCAGAAAGCTGGTTTATTGCAGCCT  927
TAACGTCCGGGTCTAGAGTCGACGGAGATAATGTGGTGATAACGTCTGCGTCGGTGTCGGGAATAATGTCGTCGGTGTCGTCTTTCGACCAAATAACGTCGGA
  L  Q  A  Q  I  S  A  A  S  I  T  P  L  L  Q  T  Q  P  Q  P  L  L  Q  Q  P  Q  Q  K  A  G  L  L  Q  P

CCTGTCCGAATAGTGTCACAGCCACAACCTGCGCGGAGATTAGATCCACCATCACGATTTTCAGGAAGAAACGACAGAGGGGATCAAGTACCTAATAGAAAAG 1030
GGACAGGCTTATCACAGTGTCGGTGTTGGACGCGCCTCTAATCTAGGTGGTAGTGCTAAAAGTCCTTCTTTGCTGTCTCCCCTAGTTCATGGATTATCTTTTC
 P  V  R  I  V  S  Q  P  Q  P  A  R  R  L  D  P  P  S  R  F  S  G  R  N  D  R  G  D  Q  V  P  N  R  K

ATGACCGAAGTCGTGAAAGGGACAGAGAAAGACGCAGATCTAGAGAAAGATCACCTCAGAGGAAACGTTCCCGGGAGAGGTCACCCCGGAGAGAAAGAGAGCG 1133
TACTGGCTTCAGCACTTTCCCTGTCTCTTTCTGCGTCTAGATCTCTTTCTAGTGGAGTCTCCTTTGCAAGGGCCCTCTCCAGTGGGGCCTCTCTTTCTCTCGC
D  D  R  S  R  E  R  D  R  E  R  R  R  S  R  E  R  S  P  Q  R  K  R  S  R  E  R  S  P  R  R  E  R  E  R

CTCCCCTCGGAGAGTCCGTCGTGTCGTTCCACGGTACACAGTGCAGTTTTCAAAGTTTTCTTTAGATTGTCCCAGTTGTGACATGATGGAACTAAGGCGCCGT 1236
GAGGGGAGCCTCTCAGGCAGCACAGCAAGGTGCCATGTGTCACGTCAAAAGTTTCAAAAGAAATCTAACAGGGTCAACACTGTACTACCTTGATTCCGCGGCA
  S  P  R  R  V  R  R  V  V  P  R  Y  T  V  Q  F  S  K  F  S  L  D  C  P  S  C  D  M  M  E  L  R  R  R

TATCAGAACTTATATATTCCTAGTGACTTTTTTGATGCTCAGTTTACATGGGTGGATGCTTTCCCTTTGTCAAGACCATTTCAACTGGGAAATTACTGCAATT 1339
ATAGTCTTGAATATATAAGGATCACTGAAAAAACTACGAGTCAAATGTACCCACCTACGAAAGGGAAACAGTTCTGGTAAAGTTGACCCTTTAATGACGTTAA
 Y  Q  N  L  Y  I  P  S  D  F  F  D  A  Q  F  T  W  V  D  A  F  P  L  S  R  P  F  Q  L  G  N  Y  C  N

TTTATGTGATGCACCGAGAAGTAGAGTCCTTAGAAAAAAATATGGCTGTTCTTGATCCACCTGATGCTGACCACCTGTACAGTGCAAAGGTAATGCTGATGGC 1442
AAATACACTACGTGGCTCTTCATCTCAGGAATCTTTTTTTATACCGACAAGAACTAGGTGGACTACGACTGGTGGACATGTCACGTTTCCATTACGACTACCG
F  Y  V  M  H  R  E  V  E  S  L  E  K  N  M  A  V  L  D  P  P  D  A  D  H  L  Y  S  A  K  V  M  L  M  A

TAGCCCTAGTATGGAAGACTTGTATCATAAGTCATGTGCTCTTGCTGAAGACCCACAAGACCTTCGTGATGGTTTTCAGCATCCTGCTAGACTTGTTAAGTTT 1545
ATCGGGATCATACCTTCTGAACATAGTATTCAGTACACGAGAACGACTTCTGGGTGTTCTGGAAGCACTACCAAAAGTCGTAGGACGATCTGAACAATTCAAA
  S  P  S  M  E  D  L  Y  H  K  S  C  A  L  A  E  D  P  Q  D  L  R  D  G  F  Q  H  P  A  R  L  V  K  F

CTAGTGGGAATGAAAGGCAAGGATGAAGCCATGGCCATTGGAGGCCACTGGTCTCCTTCGCTGGATGGACCAAACCCAGAAAAAGATCCCTCTGTGTTGATTA 1648
GATCACCCTTACTTTCCGTTCCTACTTCGGTACCGGTAACCTCCGGTGACCAGAGGAAGCGACCTACCTGGTTTGGGTCTTTTTCTAGGGAGACACAACTAAT
 L  V  G  M  K  G  K  D  E  A  M  A  I  G  G  H  W  S  P  S  L  D  G  P  N  P  E  K  D  P  S  V  L  I
```

FIG. 22C

```
AAACTGCCATTCGTTGTTGTAAGGCTCTGACAGGCATTGATCTAAGTGTATGCACACAGTGGTACCGTTTTGCAGAGATTCGCTACCATCGCCCTGAGGAGAC 1751
TTTGACGGTAAGCAACAACATTCCGAGACTGTCCGTAACTAGATTCACATACGTGTGTCACCATGGCAAAACGTCTCTAAGCGATGGTAGCGGGACTCCTCTG
K  T  A  I  R  C  C  K  A  L  T  G  I  D  L  S  V  C  T  Q  W  Y  R  F  A  E  I  R  Y  H  R  P  E  E  T

CCACAAGGGGCGTACAGTTCCAGCTCATGTGGAGACAGTGGTTTTATTTTTCCCGGATGTTTGGCATTGCCTTCCCACCCGCTCAGAGTGGGAAACCCTCTCC 1854
GGTGTTCCCCGCATGTCAAGGTCGAGTACACCTCTGTCACCAAAATAAAAAGGGCCTACAAACCGTAACGGAAGGGTGGGCGAGTCTCACCCTTTGGGAGAGG
   H  K  G  R  T  V  P  A  H  V  E  T  V  V  L  F  F  P  D  V  W  H  C  L  P  T  R  S  E  W  E  T  L  S

CGAGGATACAAGCAGCAGCTGGTCGAGAAGCTTCAGGGTGAACGCAAGAAGGCTGATGGAGAACAGGATGAAGAAGAGAAGGATGATGGTGAAGTTAAAGAGA 1957
GCTCCTATGTTCGTCGTCGACCAGCTCTTCGAAGTCCCACTTGCGTTCTTCCGACTACCTCTTGTCCTACTTCTTCTCTTCCTACTACCACTTCAATTTCTCT
  R  G  Y  K  Q  Q  L  V  E  K  L  Q  G  E  R  K  K  A  D  G  E  Q  D  E  E  E  K  D  D  G  E  V  K  E

TCGCCACTCCTACCCATTGGTCTAAGCTTGATCCAAAGGCAATGAAGGTAAATGATCTCCGAAAAGAATTAGAAAGTCGAGCTCTCAGTTCCAAAGGACTAAA 2060
AGCGGTGAGGATGGGTAACCAGATTCGAACTAGGTTTCCGTTACTTCCATTTACTAGAGGCTTTTCTTAATCTTTCAGCTCGAGAGTCAAGGTTTCCTGATTT
I  A  T  P  T  H  W  S  K  L  D  P  K  A  M  K  V  N  D  L  R  K  E  L  E  S  R  A  L  S  S  K  G  L  K

ATCGCAGTTAATAGCTCGCCTAACAAAGCAGCTTAAAATAGAAGAACAAAAAGAAGAGCAGAAGGAATTAGAGAAGTCTGAAAAGGAAGAGGAAGATGAGGAT 2163
TAGCGTCAATTATCGAGCGGATTGTTTCGTCGAATTTTATCTTCTTGTTTTTCTTCTCGTCTTCCTTAATCTCTTCAGACTTTTCCTTCTCCTTCTACTCCTA
   S  Q  L  I  A  R  L  T  K  Q  L  K  I  E  E  Q  K  E  E  Q  K  E  L  E  K  S  E  K  E  E  E  D  E  D

GATAAGAAGTCTGAGGATGATAAAGAGGAAGAAGAAAGAAAACGTCAAGAAGAAGTGGAACGACAGCGTCAAGAAAGAAGATACATTTTGCCTGATGAACCTG 2266
CTATTCTTCAGACTCCTACTATTTCTCCTTCTTCTTTCTTTTGCAGTTCTTCTTCACCTTGCTGTCGCAGTTCTTTCTTCTATGTAAAACGGACTACTTGGAC
  D  K  K  S  E  D  D  K  E  E  E  E  R  K  R  Q  E  E  V  E  R  Q  R  Q  E  R  R  Y  I  L  P  D  E  P

CCATAATTGTGCATCCGAACTGGGCTGCAAAAAGTGGCAAGTTTGATTGCAGCATCATGTCTTTGAGTGTCCTTTTGGATTACAGATTGGAAGATAATAAAGA 2369
GGTATTAACACGTAGGCTTGACCCGACGTTTTTCACCGTTCAAACTAACGTCGTAGTACAGAAACTCACAGGAAAACCTAATGTCTAACCTTCTATTATTTCT
A  I  I  V  H  P  N  W  A  A  K  S  G  K  F  D  C  S  I  M  S  L  S  V  L  L  D  Y  R  L  E  D  N  K  E

ACATTCTTTTGAGGTTTCACTGTTTGCAGAACTTTTCAATGAAATGCTTCAAAGAGACTTTGGGGTTAGAATATACAAATCATTACTCTCTCTTCCTGAGAAA 2472
TGTAAGAAAACTCCAAAGTGACAAACGTCTTGAAAAGTTACTTTACGAAGTTTCTCTGAAACCCCAATCTTATATGTTTAGTAATGAGAGAGAAGGACTCTTT
  H  S  F  E  V  S  L  F  A  E  L  F  N  E  M  L  Q  R  D  F  G  V  R  I  Y  K  S  L  L  S  L  P  E  K
```

FIG. 22D

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GAGGACAAAAAAGATAAGGAGAAGAAAAGCAAAAAAGAAGAGAGAAAAGATAAAAAAGAAGAAAGAGAAGATGATATTGATGAACCAAAACCAAAACGGAGAA 2575
CTCCTGTTTTTTCTATTCCTCTTCTTTTCGTTTTTTCTTCTCTCTTTTCTATTTTTTCTTCTTTCTCTTCTACTATAACTACTTGGTTTTGGTTTTGCCTCTT
 E  D  K  K  D  K  E  K  K  S  K  K  E  E  R  K  D  K  K  E  E  R  E  D  D  I  D  E  P  K  P  K  R  R

AATCAGGCGACGATAAAGACAAAAAAGAAGACAGAGATGAGAGAAAGAAAGAAGAAAAAAGAAAAGATGATTCTAAAGATGATGATGAAACTGAAGAAGATAA 2678
TTAGTCCGCTGCTATTTCTGTTTTTTCTTCTGTCTCTACTCTCTTTCTTTCTTCTTTTTTCTTTTCTACTAAGATTTCTACTACTACTTTGACTTCTTCTATT
K  S  G  D  D  K  D  K  K  E  D  R  D  E  R  K  K  E  E  K  R  K  D  D  S  K  D  D  D  E  T  E  E  D  N

CAATCAAGATGAGTATGACCCAATGGAGGCAGAGGAAGCTGAGGATGAAGATGACGATAGGGAGGAGGAGGAAGTAAAACGAGATGACAAAAGGGATGTCAGC 2781
GTTAGTTCTACTCATACTGGGTTACCTCCGTCTCCTTCGACTCCTACTTCTACTGCTATCCCTCCTCCTCCTTCATTTTGCTCTACTGTTTTCCCTACAGTCG
  N  Q  D  E  Y  D  P  M  E  A  E  E  A  E  D  E  D  D  D  R  E  E  E  E  V  K  R  D  D  K  R  D  V  S

CGGTACTGCAAGGACAGACCTGCGAAAGATAAGGAAAAAGAGAAGCCTCAAATGGTÇACAGTTAACAGGGATCTGCTAATGGCCTTTGTTTATTTTGATCAAA 2884
GCCATGACGTTCCTGTCTGGACGCTTTCTATTCCTTTTTCTCTTCGGAGTTTACCAGTGTCAATTGTCCCTAGACGATTACCGGAAACAAATAAAACTAGTTT
 R  Y  C  K  D  R  P  A  K  D  K  E  K  E  K  P  Q  M  V  T  V  N  R  D  L  L  M  A  F  V  Y  F  D  Q

GTCATTGCGGTTACCTTCTTGAAAAGGATTTGGAAGAAATACTATATACTCTTGGACTGCATCTTTCACGGGCTCAGGTAAAGAAACTTCTTAATAAAGTAGT 2987
CAGTAACGCCAATGGAAGAACTTTTCCTAAACCTTCTTTATGATATATGAGAACCTGACGTAGAAAGTGCCCGAGTCCATTTCTTTGAAGAATTATTTCATCA
S  H  C  G  Y  L  L  E  K  D  L  E  E  I  L  Y  T  L  G  L  H  L  S  R  A  Q  V  K  K  L  L  N  K  V  V

ACTCCGAGAATCGTGCTTTTATCGGAAATTAACAGACACCTCGAAAGATGATGAGAACCATGAAGAGTCAGAGGCACTGCAGGAAGACATGCTAGGAAACAGA 3090
TGAGGCTCTTAGCACGAAAATAGCCTTTAATTGTCTGTGGAGCTTTCTACTACTCTTGGTACTTCTCAGTCTCCGTGACGTCCTTCTGTACGATCCTTTGTCT
  L  R  E  S  C  F  Y  R  K  L  T  D  T  S  K  D  D  E  N  H  E  E  S  E  A  L  Q  E  D  M  L  G  N  R

TTATTACTTCCAACACCAACAATAAAACAGGAATCAAAAGATGGAGAGGAAAATGTAGGGCTTATTGTGTACAATGGTGCAATGGTGGATGTTGGGAGTCTCC 3193
AATAATGAAGGTTGTGGTTGTTATTTTGTCCTTAGTTTTCTACCTCTCCTTTTACATCCCGAATAACACATGTTACCACGTTACCACCTACAACCCTCAGAGG
 L  L  L  P  T  P  T  I  K  Q  E  S  K  D  G  E  E  N  V  G  L  I  V  Y  N  G  A  M  V  D  V  G  S  L

TACAAAAACTGGAAAAGAGTGAGAAAGTAAGAGCTGAGGTGGAACAGAAGCTCCAGTTACTAGAGGAGAAAACAGATGAAGATGGGAAAACTATATTAAACTT 3296
ATGTTTTTGACCTTTTCTCACTCTTTCATTCTCGACTCCACCTTGTCTTCGAGGTCAATGATCTCCTCTTTTGTCTACTTCTACCCTTTTGATATAATTTGAA
L  Q  K  L  E  K  S  E  K  V  R  A  E  V  E  Q  K  L  Q  L  L  E  E  K  T  D  E  D  G  K  T  I  L  N  L
```

FIG. 22E

```
GGAGAACTCTAACAAAAGCCTCTCTGGTGAACTTAGAGAGGTCAAAAAAGACCTTGGTCAATTACAAGAAAACCTGGAGGTTTCAGAAAACATGAATTTGCAA 3399
CCTCTTGAGATTGTTTTCGGAGAGACCACTTGAATCTCTCCAGTTTTTTCTGGAACCAGTTAATGTTCTTTTGGACCTCCAAAGTCTTTTGTACTTAAACGTT
  E  N  S  N  K  S  L  S  G  E  L  R  E  V  K  K  D  L  G  Q  L  Q  E  N  L  E  V  S  E  N  M  N  L  Q

TTTGAAAACCAATTGAATAAAACACTCAGAAACTTATCTACAGTTATGGATGATATCCACACTGTCCTCAAAAAGGATAATGTAAAGAGTGAAGACAGAGATG 3502
AAACTTTTGGTTAACTTATTTTGTGAGTCTTTGAATAGATGTCAATACCTACTATAGGTGTGACAGGAGTTTTTCCTATTACATTTCTCACTTCTGTCTCTAC
 F  E  N  Q  L  N  K  T  L  R  N  L  S  T  V  M  D  D  I  H  T  V  L  K  K  D  N  V  K  S  E  D  R  D

AGAAATCCAAGGAGAACGGCTCAGGTGTATGACACAGTGCACTTGGGGATGAGTGTGTTAATAGTGTACTATAAACAAAATAATCATGAGATGGGAATGTTTC 3605
TCTTTAGGTTCCTCTTGCCGAGTCCACATACTGTGTCACGTGAACCCCTACTCACACAATTATCACATGATATTTGTTTTATTAGTACTCTACCCTTACAAAG
E  K  S  K  E  N  G  S  G  V  .  H  S  A  L  G  D  E  C  V  N  S  V  L  .  T  K  .  S  .  D  G  N  V  S

ACGGCAGTGCATGCTTGACTTTAGTAGTATAAACATATATGTTAGTTCAAATGATGTATAAAGTTTTATGAATGTGAGTCTGCTTTTGAAAATTGCCTGTAAT 3708
TGCCGTCACGTACGAACTGAAATCATCATATTTGTATATACAATCAAGTTTACTACATATTTCAAAATACTTACACTCAGACGAAAACTTTTAACGGACATTA
  R  Q  C  M  L  D  F  S  S  I  N  I  Y  V  S  S  N  D  V  .  S  F  M  N  V  S  L  L  L  K  I  A  C  N

TTCTAGCATTCAAATTATTAAATACTCACTGAGTGAAGAATTTTGCATTGCAAAACCTTTTAGGATGAACTTGGTTATAGTTTCCCCAATAAAGTTCATCAGT 3811
AAGATCGTAAGTTTAATAATTTATGAGTGACTCACTTCTTAAAACGTAACGTTTTGGAAAATCCTACTTGAACCAATATCAAAGGGGTTATTTCAAGTAGTCA
 F  .  H  S  N  Y  .  I  L  T  E  .  R  I  L  H  C  K  T  F  .  D  E  L  G  Y  S  F  P  N  K  V  H  Q

GTCATTGACAATGACAAGTAATTAAAACCAAAAAAAAAAAAAAACAAACACCAACCAGG 3869
CAGTAACTGTTACTGTTCATTAATTTTGGTTTTTTTTTTTTTGTTTGTGGTTGGTCC
C  H  .  Q  .  Q  V  I  K  T  K  K  K  K  N  K  H  Q  P  G
```

FIG. 23A

GGGGGGTTTGAAATGGCTTCTCGGTTAACCCGGGCCAGACTCAGGTATCTGCTAT
AGAAGGGAAACAAGTGAAAGTTTTCCCCCCCTTGCATCATGGCTCAGTTTGGAGG
ACAGAAGAATCCACCATGGGCTACTCAGTTTACAGCCACTGCGGTCTCACAACCA
GCTGCACTAGGTGTTCAGCAGCCATCACTTCTGGGAGCATCTCCTACCATTTATA
CCCAGCAGACTGCATTGGCGGCGGCAGGCCTTACCACACAAACGCCAGCAAACTA
TCAGTTAACACAAACTGCGGCACTGCAGCAACAAGCTGCAGCTGTATTACAGCAG
CAATATTCACAACCTCAGCAGGCCTTGTATAGTGTGCAGCAGCAGTTGCAACAAC
CTCAGCAGACCATTTTAACACAGCCAGCTGTTGCATTGCCCACAAGCCTTAGCCT
GTCGACTCCTCAGCCTGCAGCACAGATTACTGTATCATATCCAACACCAAGGTCC
AGTCAACAGCAAACTCAACCTCAGAAGCAGCGTGTTTTCACAGGAGTGGTTACAA
AGCTACATGATACATTTGGATTTGTGGATGAAGATGTATTCTTTCAGCTTGGTGC
TGTTAAAGGGAAAACCCCCCAAGTTGGTGATAGAGTATTGGTTGAAGCAACTTAT
AATCCTAATATGCCTTTTAAATGGAATGCACAAAGAATTCAAACACTACCAAATC
AGAATCAGTCTCAAACGCAACCTTTACTGAAGACTCCGACTGCTGTTATTCAGCC
GATTGTGCCACAGACAACGTTTGGTGTTCAGGCACAGCCCCAACCCCAGTCATTA
TTGCAGGCCCAGATCTCAGCTGCCTCTATTACACCACTATTGCAGACGCAGCCAC
AGCCCTTATTACAGCAGCCACAGCAGAAAGCTGGTTTATTGCAGCCTCCTGTCCG
AATAGTGTCACAGCCACAACCTGCGCGGAGATTAGATCCACCATCACGATTTTCA
GGAAGAAACGACAGAGGGGATCAAGTACCTAATAGAAAAGATGACCGAAGTCGTG
AAAGGGACAGAGAAAGACGCAGATCTAGAGAAAGATCACCTCAGAGGAAACGTTC
CCGGGAGAGGTCACCCCGGAGAGAAAGAGAGCGCTCCCCTCGGAGAGTCCGTCGT
GTCGTTCCACGGTACACAGTGCAGTTTTCAAAGTTTTCTTTAGATTGTCCCAGTT
GTGACATGATGGAACTAAGGCGCCGTTATCAGAACTTATATATTCCTAGTGACTT
TTTTGATGCTCAGTTTACATGGGTGGATGCTTTCCCTTTGTCAAGACCATTTCAA
CTGGGAAATTACTGCAATTTTTATGTGATGCACCGAGAAGTAGAGTCCTTAGAAA
AAAATATGGCTGTTCTTGATCCACCTGATGCTGACCACCTGTACAGTGCAAAGGT
AATGCTGATGGCTAGCCCTAGTATGGAAGACTTGTATCATAAGTCATGTGCTCTT
GCTGAAGACCCACAAGACCTTCGTGATGGTTTTCAGCATCCTGCTAGACTTGTTA
AGTTTCTAGTGGGAATGAAAGGCAAGGATGAAGCCATGGCCATTGGAGGCCACTG
GTCTCCTTCGCTGGATGGACCAAACCCAGAAAAAGATCCCTCTGTGTTGATTAAA
ACTGCCATTCGTTGTTGTAAGGCTCTGACAGGCATTGATCTAAGTGTATGCACAC
AGTGGTACCGTTTTGCAGAGATTCGCTACCATCGCCCTGAGGAGACCCACAAGGG
GCGTACAGTTCCAGCTCATGTGGAGACAGTGGTTTTATTTTTCCCGGATGTTTGG
CATTGCCTTCCCACCCGCTCAGAGTGGGAAACCCTCTCCCGAGGATACAAGCAGC
AGCTGGTCGAGAAGCTTCAGGGTGAACGCAAGAAGGCTGATGGAGAACAGGATGA
AGAAGAGAAGGATGATGGTGAAGTTAAAGAGATCGCCACTCCTACCCATTGGTCT
AAGCTTGATCCAAAGGCAATGAAGGTAAATGATCTCCGAAAAGAATTAGAAAGTC
GAGCTCTCAGTTCCAAAGGACTAAAATCGCAGTTAATAGCTCGCCTAACAAAGCA
GCTTAAAATAGAAGAACAAAAAGAAGAGCAGAAGGAATTAGAGAAGTCTGAAAAG
GAAGAGGAAGATGAGGATGATAAGAAGTCTGAGGATGATAAAGAGGAAGAAGAAA
GAAAACGTCAAGAAGAAGTGGAACGACAGCGTCAAGAAAGAAGATACATTTTGCC
TGATGAACCTGCCATAATTGTGCATCCGAACTGGGCTGCAAAAAGTGGCAAGTTT

FIG. 23B

GATTGCAGCATCATGTCTTTGAGTGTCCTTTTGGATTACAGATTGGAAGATAATA
AAGAACATTCTTTTGAGGTTTCACTGTTTGCAGAACTTTTCAATGAAATGCTTCA
AAGAGACTTTGGGGTTAGAATATACAAATCATTACTCTCTCTTCCTGAGAAAGAG
GACAAAAAAGATAAGGAGAAGAAAAGCAAAAAAGAAGAGAGAAAAGATAAAAAAG
AAGAAAGAGAAGATGATATTGATGAACCAAAACCAAAACGGAGAAAATCAGGCGA
CGATAAAGACAAAAAAGAAGACAGAGATGAGAGAAAGAAAGAAGAAAAAAGAAAA
GATGATTCTAAAGATGATGATGAAACTGAAGAAGATAACAATCAAGATGAGTATG
ACCCAATGGAGGCAGAGGAAGCTGAGGATGAAGATGACGATAGGGAGGAGGAGGA
AGTAAAACGAGATGACAAAAGGGATGTCAGCCGGTACTGCAAGGACAGACCTGCG
AAAGATAAGGAAAAAGAGAAGCCTCAAATGGTCACAGTTAACAGGGATCTGCTAA
TGGCCTTTGTTTATTTTGATCAAAGTCATTGCGGTTACCTTCTTGAAAAGGATTT
GGAAGAAATACTATATACTCTTGGACTGCATCTTTCACGGGCTCAGGTAAAGAAA
CTTCTTAATAAAGTAGTACTCCGAGAATCGTGCTTTTATCGGAAATTAACAGACA
CCTCGAAAGATGATGAGAACCATGAAGAGTCAGAGGCACTGCAGGAAGACATGCT
AGGAAACAGATTATTACTTCCAACACCAACAATAAAACAGGAATCAAAAGATGGA
GAGGAAAATGTAGGGCTTATTGTGTACAATGGTGCAATGGTGGATGTTGGGAGTC
TCCTACAAAAACTGGAAAAGAGTGAGAAAGTAAGAGCTGAGGTGGAACAGAAGCT
CCAGTTACTAGAGGAGAAAACAGATGAAGATGGGAAAACTATATTAAACTTGGAG
AACTCTAACAAAAGCCTCTCTGGTGAACTTAGAGAGGTCAAAAAAGACCTTGGTC
AATTACAAGAAAACCTGGAGGTTTCAGAAAACATGAATTTGCAATTTGAAAACCA
ATTGAATAAAACACTCAGAAACTTATCTACAGTTATGGATGATATCCACACTGTC
CTCAAAAAGGATAATGTAAAGAGTGAAGACAGAGATGAGAAATCCAAGGAGAACG
GCTCAGGTGTATGACACAGTGCACTTGGGGATGAGTGTGTTAATAGTGTACTATA
AACAAAATAATCATGAGATGGGAATGTTTCACGGCAGTGCATGCTTGACTTTAGT
AGTATAAACATATATGTTAGTTCAAATGATGTATAAAGTTTTATGAATGTGAGTC
TGCTTTTGAAAATTGCCTGTAATTTCTAGCATTCAAATTATTAAATACTCACTGA
GTGAAGAATTTTGCATTGCAAAACCTTTTAGGATGAACTTGGTTATAGTTTCCCC
AATAAAGTTCATCAGTGTCATTGACAATGACAAGTAATTAAAACCAAAAAAAAAA
AAAACAAACACCAACCAGG

FIG. 24A

mDIS cDNA

GGGGGGTTTGAAATGGCTTCTCGGTTAACCCGGGCCAGACTCAGGTATCTGCTAT
AGAAGGGAAACAAGTGAAAGTTTTCCCCCCCTTGCATC

```
  94 atggctcagtttggaggacagaagaatccaccatgggctactcag
     M  A  Q  F  G  G  Q  K  N  P  P  W  A  T  Q
 139 tttacagccactgcggtctcacaaccagctgcactaggtgttcag
     F  T  A  T  A  V  S  Q  P  A  A  L  G  V  Q
 184 cagccatcacttctgggagcatctcctaccatttatacccagcag
     Q  P  S  L  L  G  A  S  P  T  I  Y  T  Q  Q
 229 actgcattggcggcggcaggccttaccacacaaacgccagcaaac
     T  A  L  A  A  A  G  L  T  T  Q  T  P  A  N
 274 tatcagttaacacaaactgcggcactgcagcaacaagctgcagct
     Y  Q  L  T  Q  T  A  A  L  Q  Q  Q  A  A  A
 319 gtattacagcagcaatattcacaacctcagcaggccttgtatagt
     V  L  Q  Q  Q  Y  S  Q  P  Q  Q  A  L  Y  S
 364 gtgcagcagcagttgcaacaacctcagcagaccattttaacacag
     V  Q  Q  Q  L  Q  Q  P  Q  Q  T  I  L  T  Q
 409 ccagctgttgcattgcccacaagccttagcctgtcgactcctcag
     P  A  V  A  L  P  T  S  L  S  L  S  T  P  Q
 454 cctgcagcacagattactgtatcatatccaacaccaaggtccagt
     P  A  A  Q  I  T  V  S  Y  P  T  P  R  S  S
 499 caacagcaaactcaacctcagaagcagcgtgttttcacaggagtg
     Q  Q  Q  T  Q  P  Q  K  Q  R  V  F  T  G  V
 544 gttacaaagctacatgatacatttggatttgtggatgaagatgta
     V  T  K  L  H  D  T  F  G  F  V  D  E  D  V
 589 ttctttcagcttggtgctgttaaagggaaaaccccccaagttggt
     F  F  Q  L  G  A  V  K  G  K  T  P  Q  V  G
 634 gatagagtattggttgaagcaacttataatcctaatatgccttttt
     D  R  V  L  V  E  A  T  Y  N  P  N  M  P  F
 679 aaatggaatgcacaaagaattcaaacactaccaaatcagaatcag
     K  W  N  A  Q  R  I  Q  T  L  P  N  Q  N  Q
 724 tctcaaacgcaacctttactgaagactccgactgctgttattcag
     S  Q  T  Q  P  L  L  K  T  P  T  A  V  I  Q
 769 ccgattgtgccacagacaacgtttggtgttcaggcacagccccaa
     P  I  V  P  Q  T  T  F  G  V  Q  A  Q  P  Q
```

FIG. 24B

814 ccccagtcattattgcaggcccagatctcagctgcctctattaca
P Q S L L Q A Q I S A A S I T
859 ccactattgcagacgcagccacagcccttattacagcagccacag
P L L Q T Q P Q P L L Q Q P Q
904 cagaaagctggtttattgcagcctcctgtccgaatagtgtcacag
Q K A G L L Q P P V R I V S Q
949 ccacaacctgcgcggagattagatccaccatcacgattttcagga
P Q P A R R L D P P S R F S G
994 agaaacgacagaggggatcaagtacctaatagaaaagatgaccga
R N D R G D Q V P N R K D D R
1039 agtcgtgaaagggacagagaaagacgcagatctagagaaagatca
S R E R D R E R R R S R E R S
1084 cctcagaggaaacgttcccgggagaggtcaccccggagagaaaga
P Q R K R S R E R S P R R E R
1129 gagcgctcccctcggagagtccgtcgtgtcgttccacggtacaca
E R S P R R V R R V V P R Y T
1174 gtgcagttttcaaagttttctttagattgtcccagttgtgac**atg**
V Q F S K F S L D C P S C D **M**
1219 **atg**gaactaaggcgccgttatcagaacttatatattcctagtgac
M E L R R R Y Q N L Y I P S D
1264 ttttttgatgctcagtttacatgggtggatgctttccctttgtca
F F D A Q F T W V D A F P L S
1309 agaccatttcaactgggaaattactgcaatttttatgtg**atg**cac
R P F Q L G N Y C N F Y V **M** H
1354 cgagaagtagagtccttagaaaaaaat**atg**gctgttcttgatcca
R E V E S L E K N **M** A V L D P
1399 cctgatgctgaccacctgtacagtgcaaaggta**atg**ctg**atg**gct
P D A D H L Y S A K V **M** L **M** A
1444 agccctagt**atg**gaagacttgtatcataagtcatgtgctcttgct
S P S **M** E D L Y H K S C A L A
1489 gaagacccacaagaccttcgtgatggttttcagcatcctgctaga
E D P Q D L R D G F Q H P A R
1534 cttgttaagtttctagtggga**atg**aaaggcaaggatgaagcc**atg**
L V K F L V G **M** K G K D E A **M**
1579 gccattggaggccactggtctccttcgctggatggaccaaaccca
A I G G H W S P S L D G P N P

FIG. 24C

```
1624 gaaaaagatccctctgtgttgattaaaactgccattcgttgttgt
     E  K  D  P  S  V  L  I  K  T  A  I  R  C  C
1669 aaggctctgacaggcattgatctaagtgtatgcacacagtggtac
     K  A  L  T  G  I  D  L  S  V  C  T  Q  W  Y
1714 cgttttgcagagattcgctaccatcgccctgaggagacccacaag
     R  F  A  E  I  R  Y  H  R  P  E  E  T  H  K
1759 gggcgtacagttccagctcatgtggagacagtggttttatttttc
     G  R  T  V  P  A  H  V  E  T  V  V  L  F  F
1804 ccggatgtttggcattgccttcccacccgctcagagtgggaaacc
     P  D  V  W  H  C  L  P  T  R  S  E  W  E  T
1849 ctctcccgaggatacaagcagcagctggtcgagaagcttcagggt
     L  S  R  G  Y  K  Q  Q  L  V  E  K  L  Q  G
1894 gaacgcaagaaggctgatggagaacaggatgaagaagagaaggat
     E  R  K  K  A  D  G  E  Q  D  E  E  E  K  D
1939 gatggtgaagttaaagagatcgccactcctacccattggtctaag
     D  G  E  V  K  E  I  A  T  P  T  H  W  S  K
1984 cttgatccaaaggcaatgaaggtaaatgatctccgaaaagaatta
     L  D  P  K  A  M  K  V  N  D  L  R  K  E  L
2029 gaaagtcgagctctcagttccaaaggactaaaatcgcagttaata
     E  S  R  A  L  S  S  K  G  L  K  S  Q  L  I
2074 gctcgcctaacaaagcagcttaaaatagaagaacaaaaagaagag
     A  R  L  T  K  Q  L  K  I  E  E  Q  K  E  E
2119 cagaaggaattagagaagtctgaaaaggaagaggaagatgaggat
     Q  K  E  L  E  K  S  E  K  E  E  E  D  E  D
2164 gataagaagtctgaggatgataaagaggaagaagaaagaaaacgt
     D  K  K  S  E  D  D  K  E  E  E  E  R  K  R
2209 caagaagaagtggaacgacagcgtcaagaaagaagatacattttg
     Q  E  E  V  E  R  Q  R  Q  E  R  R  Y  I  L
2254 cctgatgaacctgccataattgtgcatccgaactgggctgcaaaa
     P  D  E  P  A  I  I  V  H  P  N  W  A  A  K
2299 agtggcaagtttgattgcagcatcatgtctttgagtgtccttttg
     S  G  K  F  D  C  S  I  M  S  L  S  V  L  L
2344 gattacagattggaagataataaagaacattcttttgaggtttca
     D  Y  R  L  E  D  N  K  E  H  S  F  E  V  S
2389 ctgtttgcagaacttttcaatgaaatgcttcaaagagactttggg
     L  F  A  E  L  F  N  E  M  L  Q  R  D  F  G
```

FIG. 24D

2434 gttagaatatacaaatcattactctctcttcctgagaaagaggac
V R I Y K S L L S L P E K E D
2479 aaaaaagataaggagaagaaaagcaaaaaagaagagagaaaagat
K K D K E K K S K K E E R K D
2524 aaaaaagaagaaagagaagatgatattgatgaaccaaaaccaaaa
K K E E R E D D I D E P K P K
2569 cggagaaaatcaggcgacgataaagacaaaaaagaagacagagat
R R K S G D D K D K K E D R D
2614 gagagaaagaaagaagaaaaaagaaaagatgattctaaagatgat
E R K K E E K R K D D S K D D
2659 gatgaaactgaagaagataacaatcaagatgagtatgacccaatg
D E T E E D N N Q D E Y D P M
2704 gaggcagaggaagctgaggatgaagatgacgatagggaggaggag
E A E E A E D E D D D R E E E
2749 gaagtaaaacgagatgacaaaagggatgtcagccggtactgcaag
E V K R D D K R D V S R Y C K
2794 gacagacctgcgaaagataaggaaaaagagaagcctcaaatggtc
D R P A K D K E K E K P Q M V
2839 acagttaacagggatctgctaatggcctttgtttattttgatcaa
T V N R D L L M A F V Y F D Q
2884 agtcattgcggttaccttcttgaaaaggatttggaagaaatacta
S H C G Y L L E K D L E E I L
2929 tatactcttggactgcatctttcacgggctcaggtaaagaaactt
Y T L G L H L S R A Q V K K L
2974 cttaataaagtagtactccgagaatcgtgcttttatcggaaatta
L N K V V L R E S C F Y R K L
3019 acagacacctcgaaagatgatgagaaccatgaagagtcagaggca
T D T S K D D E N H E E S E A
3064 ctgcaggaagacatgctaggaaacagattattacttccaacacca
L Q E D M L G N R L L L P T P
3109 acaataaaacaggaatcaaaagatggagaggaaaatgtagggctt
T I K Q E S K D G E E N V G L
3154 attgtgtacaatggtgcaatggtggatgttgggagtctcctacaa
I V Y N G A M V D V G S L L Q
3199 aaactggaaaagagtgagaaagtaagagctgaggtggaacagaag
K L E K S E K V R A E V E Q K

FIG. 13E

```
3244 ctccagttactagaggagaaaacagatgaagatgggaaaactata
     L  Q  L  L  E  E  K  T  D  E  D  G  K  T  I
3289 ttaaacttggagaactctaacaaaagcctctctggtgaacttaga
     L  N  L  E  N  S  N  K  S  L  S  G  E  L  R
3334 gaggtcaaaaaagaccttggtcaattacaagaaaacctggaggtt
     E  V  K  K  D  L  G  Q  L  Q  E  N  L  E  V
3379 tcagaaaacatgaatttgcaatttgaaaaccaattgaataaaaca
     S  E  N  M  N  L  Q  F  E  N  Q  L  N  K  T
3424 ctcagaaacttatctacagttatggatgatatccacactgtcctc
     L  R  N  L  S  T  V  M  D  D  I  H  T  V  L
3469 aaaaaggataatgtaaagagtgaagacagagatgagaaatccaag
     K  K  D  N  V  K  S  E  D  R  D  E  K  S  K
3514 gagaacggctcaggtgtatga 3534
     E  N  G  S  G  V  *
```

CACAGTGCACTTGGGGATGAGTGTGTTAATAGTGTACTATAAACAAAATAATCAT
GAGATGGGAATGTTTCACGGCAGTGCATGCTTGACTTTAGTAGTATAAACATATA
TGTTAGTTCAAATGATGTATAAAGTTTTATGAATGTGAGTCTGCTTTTGAAAATT
GCCTGTAATTTCTAGCATTCAAATTATTAAATACTCACTGAGTGAAGAATTTTGC
ATTGCAAAACCTTTTAGGATGAACTTGGTTATAGTTTCCCCAATAAAGTTCATCA
GTGTCATTGACAATGACAAGTAATTAAAACCAAAAAAAAAAAAAACAAACACCAA
CCAGG

FIG. 25A

```
GAAGTTGGCGCATGCGCCTAAAGCTGACGGGTTTGAAATGGCTTCGATGTTAGCCGGGACCCGACTCAGATCGATGCTATAGAAGACAAACAAGGAAAGGTTT  103
CTTCAACCGCGTACGCGGATTTCGACTGCCCAAACTTTACCGAAGCTACAATCGGCCCTGGGCTGAGTCTAGCTACGATATCTTCTGTTTGTTCCTTTCCAAA
.  S  W  R  M  R  L  K  L  T  G  L  K  W  L  R  C  .  P  G  P  D  S  D  R  C  Y  R  R  Q  T  R  K  G  F

TTTTTCCTTTTGCATCATGGCTCAATTTGGAGGACAGAAGAATCCGCCATGGGCTACTCAGTTTACAGCCACTGCAGTATCACAGCCAGCTGCACTGGGTGTT  206
AAAAAGGAAAACGTAGTACCGAGTTAAACCTCCTGTCTTCTTAGGCGGTACCCGATGAGTCAAATGTCGGTGACGTCATAGTGTCGGTCGACGTGACCCACAA
  F  S  F  C  I  M  A  Q  F  G  G  Q  K  N  P  P  W  A  T  Q  F  T  A  T  A  V  S  Q  P  A  A  L  G  V

CAACAGCCATCACTCCTTGGAGCATCTCCTACCATTTATACACAGCAAACTGCATTGGCAGCAGCAGGCCTTACCACACAAACTCCAGCAAACTATCAGTTAA  309
GTTGTCGGTAGTGAGGAACCTCGTAGAGGATGGTAAATATGTGTCGTTTGACGTAACCGTCGTCGTCCGGAATGGTGTGTTTGAGGTCGTTTGATAGTCAATT
  Q  Q  P  S  L  L  G  A  S  P  T  I  Y  T  Q  Q  T  A  L  A  A  A  G  L  T  T  Q  T  P  A  N  Y  Q  L

CACAAACTGCTGCATTGCAGCAACAAGCCGCAGCTGCAGCAGCTGCATTACAACAGCAATATTCACAACCTCAGCAGGCCCTGTATAGTGTGCAACAACAGTT  412
GTGTTTGACGACGTAACGTCGTTGTTCGGCGTCGACGTCGTCGACGTAATGTTGTCGTTATAAGTGTTGGAGTCGTCCGGGACATATCACACGTTGTTGTCAA
T  Q  T  A  A  L  Q  Q  Q  A  A  A  A  A  A  A  L  Q  Q  Q  Y  S  Q  P  Q  Q  A  L  Y  S  V  Q  Q  Q  L

ACAGCAACCCCAGCAAACCCTCTTAACACAGCCAGCTGTTGCACTGCCTACAAGCCTTAGCCTGTCTACTCCTCAGCCAACAGCACAAATAACTGTATCATAT  515
TGTCGTTGGGGTCGTTTGGGAGAATTGTGTCGGTCGACAACGTGACGGATGTTCGGAATCGGACAGATGAGGAGTCGGTTGTCGTGTTTATTGACATAGTATA
  Q  Q  P  Q  Q  T  L  L  T  Q  P  A  V  A  L  P  T  S  L  S  L  S  T  P  Q  P  T  A  Q  I  T  V  S  Y

CCAACACCAAGGTCCAGTCAACAGCAAACCCAGCCTCAGAAGCAGCGTGTTTTCACAGGGGTGGTTACAAAACTACATGATACATTTGGATTTGTGGATGAAG  618
GGTTGTGGTTCCAGGTCAGTTGTCGTTTGGGTCGGAGTCTTCGTCGCACAAAAGTGTCCCCACCAATGTTTTGATGTACTATGTAAACCTAAACACCTACTTC
  P  T  P  R  S  S  Q  Q  Q  T  Q  P  Q  K  Q  R  V  F  T  G  V  V  T  K  L  H  D  T  F  G  F  V  D  E

ATGTATTCTTTCAGCTTAGTGCTGTCAAAGGGAAAACCCCCCAAGTAGGTGACAGAGTATTGGTTGAAGCTACTTATAATCCTAATATGCCTTTTAAATGGAA  721
TACATAAGAAAGTCGAATCACGACAGTTTCCCTTTTGGGGGGTTCATCCACTGTCTCATAACCAACTTCGATGAATATTAGGATTATACGGAAAATTTACCTT
D  V  F  F  Q  L  S  A  V  K  G  K  T  P  Q  V  G  D  R  V  L  V  E  A  T  Y  N  P  N  M  P  F  K  W  N

TGCACAGAGAATTCAAACACTACCAAATCAGAATCAGTCGCAAACCCAGCCATTACTGAAGACTCCTCCTGCTGTACTTCAGCCAATTGCACCACAGACAACA  824
ACGTGTCTCTTAAGTTTGTGATGGTTTAGTCTTAGTCAGCGTTTGGGTCGGTAATGACTTCTGAGGAGGACGACATGAAGTCGGTTAACGTGGTGTCTGTTGT
  A  Q  R  I  Q  T  L  P  N  Q  N  Q  S  Q  T  Q  P  L  L  K  T  P  P  A  V  L  Q  P  I  A  P  Q  T  T
```

FIG. 25B

```
TTTGGTGTTCAGACTCAGCCCCAGCCCCAGTCACTGCTGCAGGCACAGATTTCAGCAGCTTCTATTACACCACTATTGCAGACTCAACCACAGCCCTTATTAC  927
AAACCACAAGTCTGAGTCGGGGTCGGGGTCAGTGACGACGTCCGTGTCTAAAGTCGTCGAAGATAATGTGGTGATAACGTCTGAGTTGGTGTCGGGAATAATG
 F  G  V  Q  T  Q  P  Q  P  Q  S  L  L  Q  A  Q  I  S  A  A  S  I  T  P  L  L  Q  T  Q  P  Q  P  L  L

AGCAGCCTCAGCAAAAAGCTGGTTTATTGCAGCCTCCTGTTCGTATAGTTTCACAGCCACAACCGGCACGACGATTAGATCCCCCATCCCGATTTTCAGGAAG 1030
TCGTCGGAGTCGTTTTTCGACCAAATAACGTCGGAGGACAAGCATATCAAAGTGTCGGTGTTGGCCGTGCTGCTAATCTAGGGGGTAGGGCTAAAAGTCCTTC
Q  Q  P  Q  Q  K  A  G  L  L  Q  P  P  V  R  I  V  S  Q  P  Q  P  A  R  R  L  D  P  P  S  R  F  S  G  R

AAATGACAGAGGGGATCAAGTGCCTAACAGAAAAGATGATCGAAGTCGTGAGAGAGAGAGAGAAAGACGTAGATCGAGAGAAAGATCACCTCAGAGGAAACGT 1133
TTTACTGTCTCCCCTAGTTCACGGATTGTCTTTTCTACTAGCTTCAGCACTCTCTCTCTCTCTTTCTGCATCTAGCTCTCTTTCTAGTGGAGTCTCCTTTGCA
  N  D  R  G  D  Q  V  P  N  R  K  D  D  R  S  R  E  R  E  R  E  R  R  R  S  R  E  R  S  P  Q  R  K  R

TCCCGGGAAAGATCTCCACGAAGAGAGCGAGAGCGATCACCTCGGAGAGTTCGACGTGTTGTTCCACGTTACACAGTTCAGTTTTCAAAGTTTTCTTTAGATT 1236
AGGGCCCTTTCTAGAGGTGCTTCTCTCGCTCTCGCTAGTGGAGCCTCTCAAGCTGCACAACAAGGTGCAATGTGTCAAGTCAAAAGTTTCAAAAGAAATCTAA
 S  R  E  R  S  P  R  R  E  R  E  R  S  P  R  R  V  R  R  V  V  P  R  Y  T  V  Q  F  S  K  F  S  L  D

GTCCCAGTTGTGACATGATGGAACTAAGGCGCCGTTATCAAAATTTGTATATACCTAGTGACTTTTTTGATGCTCAATTTACATGGGTGGATGCTTTCCCTTT 1339
CAGGGTCAACACTGTACTACCTTGATTCCGCGGCAATAGTTTTAAACATATATGGATCACTGAAAAAACTACGAGTTAAATGTACCCACCTACGAAAGGGAAA
C  P  S  C  D  M  M  E  L  R  R  R  Y  Q  N  L  Y  I  P  S  D  F  F  D  A  Q  F  T  W  V  D  A  F  P  L

GTCAAGACCATTTCAGCTGGGAAATTACTGCAATTTTTATGTAATGCACAGAGAAGTAGAGTCCTTAGAAAAAAATATGGCCATTCTTGATCCACCAGATGCT 1442
CAGTTCTGGTAAAGTCGACCCTTTAATGACGTTAAAAATACATTACGTGTCTCTTCATCTCAGGAATCTTTTTTTATACCGGTAAGAACTAGGTGGTCTACGA
  S  R  P  F  Q  L  G  N  Y  C  N  F  Y  V  M  H  R  E  V  E  S  L  E  K  N  M  A  I  L  D  P  P  D  A

GACCACTTATACAGTGCAAAGGTAATGCTGATGGCTAGCCCTAGTATGGAAGATTTATATCATAAGTCATGTGCTCTTGCTGAGGACCCACAAGAACTTCGAG 1545
CTGGTGAATATGTCACGTTTCCATTACGACTACCGATCGGGATCATACCTTCTAAATATAGTATTCAGTACACGAGAACGAGTCCTGGGTGTTCTTGAAGCTC
 D  H  L  Y  S  A  K  V  M  L  M  A  S  P  S  M  E  D  L  Y  H  K  S  C  A  L  A  E  D  P  Q  E  L  R

ATGGATTCCAACATCCTGCTAGACTTGTTAAGTTTTTAGTGGGCATGAAAGGCAAGGATGAAGCTATGGCCATTGGAGGCCACTGGTCTCCTTCGTTGGATGG 1648
TACCTAAGGTTGTAGGACGATCTGAACAATTCAAAAATCACCCGTACTTTCCGTTCCTACTTCGATACCGGTAACCTCCGGTGACCAGAGGAAGCAACCTACC
D  G  F  Q  H  P  A  R  L  V  K  F  L  V  G  M  K  G  K  D  E  A  M  A  I  G  G  H  W  S  P  S  L  D  G
```

FIG. 25C

```
ACCAGACCCAGAAAAAGATCCCTCTGTGTTGATTAAGACTGCTATTCGTTGTTGTAAGGCTCTGACAGGCATTGATCTAAGTGTGTGCACACAATGGTACCGT 1751
TGGTCTGGGTCTTTTTCTAGGGAGACACAACTAATTCTGACGATAAGCAACAACATTCCGAGACTGTCCGTAACTAGATTCACACACGTGTGTTACCATGGCA
  P  D  P  E  K  D  P  S  V  L  I  K  T  A  I  R  C  C  K  A  L  T  G  I  D  L  S  V  C  T  Q  W  Y  R

TTTGCAGAGATTCGCTACCATCGCCCTGAGGAGACCCACAAGGGGCGTACAGTTCCAGCTCATGTGGAGACAGTGGTTTTATTTTTCCCGGATGTTTGGCATT 1854
AAACGTCTCTAAGCGATGGTAGCGGGACTCCTCTGGGTGTTCCCCGCATGTCAAGGTCGAGTACACCTCTGTCACCAAAATAAAAAGGGCCTACAAACCGTAA
 F  A  E  I  R  Y  H  R  P  E  E  T  H  K  G  R  T  V  P  A  H  V  E  T  V  V  L  F  F  P  D  V  W  H

GCCTTCCCACCCGCTCAGAGTGGGAAACCCTCTCCCGAGGATACAAGCAGCAGCTGGTCGAGAAGCTTCAGGGTGAACGCAAGGAGGCTGATGGAGAACAGGA 1957
CGGAAGGGTGGGCGAGTCTCACCCTTTGGGAGAGGGCTCCTATGTTCGTCGTCGACCAGCTCTTCGAAGTCCCACTTGCGTTCCTCCGACTACCTCTTGTCCT
C  L  P  T  R  S  E  W  E  T  L  S  R  G  Y  K  Q  Q  L  V  E  K  L  Q  G  E  R  K  E  A  D  G  E  Q  D

TGAAGAAGAGAAGGATGATGGTGAAGCTAAAGAAATTTCTACACCTACCCATTGGTCTAAACTTGATCCAAAGACAATGAAGGTAAATGACCTCCGAAAAGAA 2060
ACTTCTTCTCTTCCTACTACCACTTCGATTTCTTTAAAGATGTGGATGGGTAACCAGATTTGAACTAGGTTTCTGTTACTTCCATTTACTGGAGGCTTTTCTT
  E  E  E  K  D  D  G  E  A  K  E  I  S  T  P  T  H  W  S  K  L  D  P  K  T  M  K  V  N  D  L  R  K  E

TTAGAAGGTCGAGCTCTTAGTTCCAAAGGATTAAAATCCCAGTTAATAGCCCGATTGACAAAACAGCTTAAAGTAGAGGAACAAAAAGAAGAACAGAAGGAGT 2163
AATCTTCCAGCTCGAGAATCAAGGTTTCCTAATTTTAGGGTCAATTATCGGGCTAACTGTTTTGTCGAATTTCATCTCCTTGTTTTTCTTCTTGTCTTCCTCA
 L  E  G  R  A  L  S  S  K  G  L  K  S  Q  L  I  A  R  L  T  K  Q  L  K  V  E  E  Q  K  E  E  Q  K  E

TAGAGAAATCTGAAAAAGAAGAGGATGAGGATGATGATAGGAAATCTGAAGACGATAAAGAGGAAGAAGAAAGGAAACGTCAAGAGGAAATAGAACGCCAGCG 2266
ATCTCTTTAGACTTTTTCTTCTCCTACTCCTACTACTATCCTTTAGACTTCTGCTATTTCTCCTTCTTCTTTCCTTTGCAGTTCTCCTTTATCTTGCGGTCGC
L  E  K  S  E  K  E  E  D  E  D  D  D  R  K  S  E  D  D  K  E  E  E  E  R  K  R  Q  E  E  I  E  R  Q  R

TCGAGAAAGAAGATATATTTTGCCTGATGAACCGGCCATCATTGTACATCCAAATTGGGCTGCAAAAAGTGGCAAGTTTGATTGTAGCATCATGTCTTTGAGT 2369
AGCTCTTTCTTCTATATAAAACGGACTACTTGGCCGGTAGTAACATGTAGGTTTAACCCGACGTTTTTCACCGTTCAAACTAACATCGTAGTACAGAAACTCA
  R  E  R  R  Y  I  L  P  D  E  P  A  I  I  V  H  P  N  W  A  A  K  S  G  K  F  D  C  S  I  M  S  L  S

GTCCTATTGGACTACAGATTAGAGGATAATAAAGAACATTCATTTGAGGTTTCATTGTTTGCGGAACTTTTCAACGAAATGCTTCAAAGAGATTTTGGTGTCC 2472
CAGGATAACCTGATGTCTAATCTCCTATTATTTCTTGTAAGTAAACTCCAAAGTAACAAACGCCTTGAAAAGTTGCTTTACGAAGTTTCTCTAAAACCACAGG
 V  L  L  D  Y  R  L  E  D  N  K  E  H  S  F  E  V  S  L  F  A  E  L  F  N  E  M  L  Q  R  D  F  G  V
```

FIG. 25D

```
GTATATACAAATCATTACTGTCTCTTCCTGAGAAAGAGGACAAAAAAGAAAAGGATAAAAAAAGCAAAAAAGATGAGAGAAAAGATAAAAAAGAAGAAAGAGA 2575
CATATATGTTTAGTAATGACAGAGAAGGACTCTTTCTCCTGTTTTTTCTTTTCCTATTTTTTTCGTTTTTTCTACTCTCTTTTCTATTTTTTCTTCTTTCTCT
R  I  Y  K  S  L  L  S  L  P  E  K  E  D  K  K  E  K  D  K  K  S  K  K  D  E  R  K  D  K  K  E  E  R  D

TGATGAAACTGATGAACCAAAACCCAAACGGAGAAAATCAGGCGATGATAAAGATAAAAAAGAAGATAGAGATGAAAGGAAGAAAGAAGATAAAAGAAAAGGT 2678
ACTACTTTGACTACTTGGTTTTGGGTTTGCCTCTTTTAGTCCGCTACTATTTCTATTTTTTCTTCTATCTCTACTTTCCTTCTTTCTTCTATTTTCTTTTCCA
   D  E  T  D  E  P  K  P  K  R  R  K  S  G  D  D  K  D  K  K  E  D  R  D  E  R  K  K  E  D  K  R  K  G

GATTCTAAAGATGATGATGAAACTGAAGAAGATAACAATCAAGATGAATATGACCCTATGGAAGCAGAAGAAGCTGAGGATGAAGAAGATGATAGGGATGAGG 2781
CTAAGATTTCTACTACTACTTTGACTTCTTCTATTGTTAGTTCTACTTATACTGGGATACCTTCGTCTTCTTCGACTCCTACTTCTTCTACTATCCCTACTCC
 D  S  K  D  D  D  E  T  E  E  D  N  N  Q  D  E  Y  D  P  M  E  A  E  E  A  E  D  E  E  D  D  R  D  E

AAGAAATGACCAAACGAGATGACAAAAGAGATATCAACAGATACTGCAAGGAGAGGCCCTCTAAAGATAAGGAAAAAGAAAAGACTCAAATGATCACAATTAA 2884
TTCTTTACTGGTTTGCTCTACTGTTTTCTCTATAGTTGTCTATGACGTTCCTCTCCGGGAGATTTCTATTCCTTTTTCTTTTCTGAGTTTACTAGTGTTAATT
E  E  M  T  K  R  D  D  K  R  D  I  N  R  Y  C  K  E  R  P  S  K  D  K  E  K  E  K  T  Q  M  I  T  I  N

CAGAGATCTGTTAATGGCTTTTGTTTATTTTGATCAAAGTCATTGTGGTTACCTTCTTGAAAAGGATTTGGAAGAAATACTTTATACTCTTGGACTACATCTT 2987
GTCTCTAGACAATTACCGAAAACAAATAAAACTAGTTTCAGTAACACCAATGGAAGAACTTTTCCTAAACCTTCTTTATGAAATATGAGAACCTGATGTAGAA
  R  D  L  L  M  A  F  V  Y  F  D  Q  S  H  C  G  Y  L  L  E  K  D  L  E  E  I  L  Y  T  L  G  L  H  L

TCTCGGGCTCAGGTAAAGAAGCTTCTTAATAAAGTAGTGCTCCGTGAATCTTGCTTTTACCGGAAATTAACAGACACCTCAAAAGATGAAGAGAACCATGAAG 3090
AGAGCCCGAGTCCATTTCTTCGAAGAATTATTTCATCACGAGGCACTTAGAACGAAAATGGCCTTTAATTGTCTGTGGAGTTTTCTACTTCTCTTGGTACTTC
 S  R  A  Q  V  K  K  L  L  N  K  V  V  L  R  E  S  C  F  Y  R  K  L  T  D  T  S  K  D  E  E  N  H  E

AGTCTGAGTCATTGCAGGAAGATATGCTAGGAAACAGATTATTACTTCCAACACCAACAGTAAAGCAGGAATCAAAGGATGTGGAAGAAAATGTTGGCCTCAT 3193
TCAGACTCAGTAACGTCCTTCTATACGATCCTTTGTCTAATAATGAAGGTTGTGGTTGTCATTTCGTCCTTAGTTTCCTACACCTTCTTTTACAACCGGAGTA
E  S  E  S  L  Q  E  D  M  L  G  N  R  L  L  L  P  T  P  T  V  K  Q  E  S  K  D  V  E  E  N  V  G  L  I

TGTGTACAATGGTGCAATGGTAGATGTAGGAAGCCTCTTGCAAAAATTGGAAAAGAGCGAAAAAGTAAGAGCTGAGGTAGAACAGAAGCTGCAGTTACTAGAA 3296
ACACATGTTACCACGTTACCATCTACATCCTTCGGAGAACGTTTTTAACCTTTTCTCGCTTTTTCATTCTCGACTCCATCTTGTCTTCGACGTCAATGATCTT
 V  Y  N  G  A  M  V  D  V  G  S  L  L  Q  K  L  E  K  S  E  K  V  R  A  E  V  E  Q  K  L  Q  L  L  E
```

FIG. 25E

```
GAAAAAACAGATGAAGATGAAAAAACCATATTAAATTTGGAGAATTCCAACAAAAGCCTCTCTGGTGAACTCAGAGAAGTTAAAAAGGACCTTAGTCAGTTAC 3399
CTTTTTTGTCTACTTCTACTTTTTTGGTATAATTTAAACCTCTTAAGGTTGTTTTCGGAGAGACCACTTGAGTCTCTTCAATTTTTCCTGGAATCAGTCAATG
 E  K  T  D  E  D  E  K  T  I  L  N  L  E  N  S  N  K  S  L  S  G  E  L  R  E  V  K  K  D  L  S  Q  L

AAGAAAACTTAAAGATTTCAGAAAACATGAGTTTACAATTTGAAAACCAAATGAATAAGACAATCAGAAACTTATCTACGGTAATGGATGAAATCCACACTGT 3502
TTCTTTTGAATTTCTAAAGTCTTTTGTACTCAAATGTTAAACTTTTGGTTTACTTATTCTGTTAGTCTTTGAATAGATGCCATTACCTACTTTAGGTGTGACA
Q  E  N  L  K  I  S  E  N  M  S  L  Q  F  E  N  Q  M  N  K  T  I  R  N  L  S  T  V  M  D  E  I  H  T  V

TCTCAAGAAGGATAATGTAAAGAATGAAGACAAAGATCAAAAATCCAAGGAGAATGGTGCCAGTGTATGATAAAATCCATGTAGTGATGAGGAATGGTGTTAA 3605
AGAGTTCTTCCTATTACATTTCTTACTTCTGTTTCTAGTTTTTAGGTTCCTCTTACCACGGTCACATACTATTTTAGGTACATCACTACTCCTTACCACAATT
 L  K  K  D  N  V  K  N  E  D  K  D  Q  K  S  K  E  N  G  A  S  V  .  .  N  P  C  S  D  E  E  W  C  .

ATAATGTAATATATAAAAATCATGATATAAGAATGTTTGAAGGTGATGCATGTTTGATTTTAGTAGTATAAATGTATTTTAGTTCAAATGATGTATAAAGTTT 3708
TATTACATTATATATTTTTAGTACTATATTCTTACAAACTTCCACTACGTACAAACTAAAATCATCATATTTACATAAAATCAAGTTTACTACATATTTCAAA
 I  M  .  Y  I  K  I  M  I  .  E  C  L  K  V  M  H  V  .  F  .  .  Y  K  C  I  L  V  Q  M  M  Y  K  V

TATGAATGTGAGTTTCTGCTTTTGAAAATTGCTTGTAATTCCTAGCCTTCAAATTATTAAACACTCCTTGAGTGAAATAATTTTGCATTGCAAAGTGTTTTAG 3811
ATACTTACACTCAAAGACGAAAACTTTTAACGAACATTAAGGATCGGAAGTTTAATAATTTGTGAGGAACTCACTTTATTAAAACGTAACGTTTCACAAAATC
L  .  M  .  V  S  A  F  E  N  C  L  .  F  L  A  F  K  L  L  N  T  P  .  V  K  .  F  C  I  A  K  C  F  R

GATGAACTTTGTTATAGTTTTAACTCCAATAAAGTTCATCAGTTT 3856
CTACTTGAAACAATATCAAAATTGAGGTTATTTCAAGTAGTCAAA
 M  N  F  V  I  V  L  T  P  I  K  F  I  S  L
```

FIG. 26A

GAAGTTGGCGCATGCGCCTAAAGCTGACGGGTTTGAAATGGCTTCGATGTTAGCC
GGGACCCGACTCAGATCGATGCTATAGAAGACAAACAAGGAAAGGTTTTTTTTCC
TTTTGCATCATGGCTCAATTTGGAGGACAGAAGAATCCGCCATGGGCTACTCAGT
TTACAGCCACTGCAGTATCACAGCCAGCTGCACTGGGTGTTCAACAGCCATCACT
CCTTGGAGCATCTCCTACCATTTATACACAGCAAACTGCATTGGCAGCAGCAGGC
CTTACCACACAAACTCCAGCAAACTATCAGTTAACACAAACTGCTGCATTGCAGC
AACAAGCCGCAGCTGCAGCAGCTGCATTACAACAGCAATATTCACAACCTCAGCA
GGCCCTGTATAGTGTGCAACAACAGTTACAGCAACCCCAGCAAACCCTCTTAACA
CAGCCAGCTGTTGCACTGCCTACAAGCCTTAGCCTGTCTACTCCTCAGCCAACAG
CACAAATAACTGTATCATATCCAACACCAAGGTCCAGTCAACAGCAAACCCAGCC
TCAGAAGCAGCGTGTTTTCACAGGGGTGGTTACAAAACTACATGATACATTTGGA
TTTGTGGATGAAGATGTATTCTTTCAGCTTAGTGCTGTCAAAGGGAAAACCCCCC
AAGTAGGTGACAGAGTATTGGTTGAAGCTACTTATAATCCTAATATGCCTTTTAA
ATGGAATGCACAGAGAATTCAAACACTACCAAATCAGAATCAGTCGCAAACCCAG
CCATTACTGAAGACTCCTCCTGCTGTACTTCAGCCAATTGCACCACAGACAACAT
TTGGTGTTCAGACTCAGCCCCAGCCCCAGTCACTGCTGCAGGCACAGATTTCAGC
AGCTTCTATTACACCACTATTGCAGACTCAACCACAGCCCTTATTACAGCAGCCT
CAGCAAAAAGCTGGTTTATTGCAGCCTCCTGTTCGTATAGTTTCACAGCCACAAC
CGGCACGACGATTAGATCCCCCATCCCGATTTTCAGGAAGAAATGACAGAGGGGA
TCAAGTGCCTAACAGAAAAGATGATCGAAGTCGTGAGAGAGAGAGAGAAAGACGT
AGATCGAGAGAAAGATCACCTCAGAGGAAACGTTCCCGGGAAAGATCTCCACGAA
GAGAGCGAGAGCGATCACCTCGGAGAGTTCGACGTGTTGTTCCACGTTACACAGT
TCAGTTTTCAAAGTTTTCTTTAGATTGTCCCAGTTGTGACATGATGGAACTAAGG
CGCCGTTATCAAAATTTGTATATACCTAGTGACTTTTTTGATGCTCAATTTACAT
GGGTGGATGCTTTCCCTTTGTCAAGACCATTTCAGCTGGGAAATTACTGCAATTT
TTATGTAATGCACAGAGAAGTAGAGTCCTTAGAAAAAAATATGGCCATTCTTGAT
CCACCAGATGCTGACCACTTATACAGTGCAAAGGTAATGCTGATGGCTAGCCCTA
GTATGGAAGATTTATATCATAAGTCATGTGCTCTTGCTGAGGACCCACAAGAACT
TCGAGATGGATTCCAACATCCTGCTAGACTTGTTAAGTTTTTAGTGGGCATGAAA
GGCAAGGATGAAGCTATGGCCATTGGAGGCCACTGGTCTCCTTCGTTGGATGGAC
CAGACCCAGAAAAAGATCCCTCTGTGTTGATTAAGACTGCTATTCGTTGTTGTAA
GGCTCTGACAGGCATTGATCTAAGTGTGTGCACACAATGGTACCGTTTTGCAGAG
ATTCGCTACCATCGCCCTGAGGAGACCCACAAGGGGCGTACAGTTCCAGCTCATG
TGGAGACAGTGGTTTTATTTTTCCCGGATGTTTGGCATTGCCTTCCCACCCGCTC
AGAGTGGGAAACCCTCTCCCGAGGATACAAGCAGCAGCTGGTCGAGAAGCTTCAG
GGTGAACGCAAGGAGGCTGATGGAGAACAGGATGAAGAAGAGAAGGATGATGGTG
AAGCTAAAGAAATTTCTACACCTACCCATTGGTCTAAACTTGATCCAAAGACAAT
GAAGGTAAATGACCTCCGAAAAGAATTAGAAGGTCGAGCTCTTAGTTCCAAAGGA
TTAAAATCCCAGTTAATAGCCCGATTGACAAAACAGCTTAAAGTAGAGGAACAAA
AAGAAGAACAGAAGGAGTTAGAGAAATCTGAAAAAGAAGAGGATGAGGATGATGA
TAGGAAATCTGAAGACGATAAAGAGGAAGAAGAAAGGAAACGTCAAGAGGAAATA

FIG. 26B

GAACGCCAGCGTCGAGAAAGAAGATATATTTTGCCTGATGAACCGGCCATCATTG
TACATCCAAATTGGGCTGCAAAAAGTGGCAAGTTTGATTGTAGCATCATGTCTTT
GAGTGTCCTATTGGACTACAGATTAGAGGATAATAAAGAACATTCATTTGAGGTT
TCATTGTTTGCGGAACTTTTCAACGAAATGCTTCAAAGAGATTTTGGTGTCCGTA
TATACAAATCATTACTGTCTCTTCCTGAGAAAGAGGACAAAAAAGAAAAGGATAA
AAAAAGCAAAAAAGATGAGAGAAAAGATAAAAAAGAAGAAAGAGATGATGAAACT
GATGAACCAAAACCCAAACGGAGAAAATCAGGCGATGATAAAGATAAAAAAGAAG
ATAGAGATGAAAGGAAGAAAGAAGATAAAAGAAAAGGTGATTCTAAAGATGATGA
TGAAACTGAAGAAGATAACAATCAAGATGAATATGACCCTATGGAAGCAGAAGAA
GCTGAGGATGAAGAAGATGATAGGGATGAGGAAGAAATGACCAAACGAGATGACA
AAAGAGATATCAACAGATACTGCAAGGAGAGGCCCTCTAAAGATAAGGAAAAAGA
AAAGACTCAAATGATCACAATTAACAGAGATCTGTTAATGGCTTTTGTTTATTTT
GATCAAAGTCATTGTGGTTACCTTCTTGAAAAGGATTTGGAAGAAATACTTTATA
CTCTTGGACTACATCTTTCTCGGGCTCAGGTAAAGAAGCTTCTTAATAAAGTAGT
GCTCCGTGAATCTTGCTTTTACCGGAAATTAACAGACACCTCAAAAGATGAAGAG
AACCATGAAGAGTCTGAGTCATTGCAGGAAGATATGCTAGGAAACAGATTATTAC
TTCCAACACCAACAGTAAAGCAGGAATCAAAGGATGTGGAAGAAAATGTTGGCCT
CATTGTGTACAATGGTGCAATGGTAGATGTAGGAAGCCTCTTGCAAAAATTGGAA
AAGAGCGAAAAAGTAAGAGCTGAGGTAGAACAGAAGCTGCAGTTACTAGAAGAAA
AAACAGATGAAGATGAAAAAACCATATTAAATTTGGAGAATTCCAACAAAAGCCT
CTCTGGTGAACTCAGAGAAGTTAAAAAGGACCTTAGTCAGTTACAAGAAAACTTA
AAGATTTCAGAAAACATGAGTTTACAATTTGAAAACCAAATGAATAAGACAATCA
GAAACTTATCTACGGTAATGGATGAAATCCACACTGTTCTCAAGAAGGATAATGT
AAAGAATGAAGACAAAGATCAAAAATCCAAGGAGAATGGTGCCAGTGTATGATAA
AATCCATGTAGTGATGAGGAATGGTGTTAAATAATGTAATATATAAAAATCATGA
TATAAGAATGTTTGAAGGTGATGCATGTTTGATTTTAGTAGTATAAATGTATTTT
AGTTCAAATGATGTATAAAGTTTTATGAATGTGAGTTTCTGCTTTTGAAAATTGC
TTGTAATTCCTAGCCTTCAAATTATTAAACACTCCTTGAGTGAAATAATTTTGCA
TTGCAAAGTGTTTTAGGATGAACTTTGTTATAGTTTTAACTCCAATAAAGTTCAT
CAGTTT

FIG. 27A

hDIS cDNA

GAAGTTGGCGCATGCGCCTAAAGCTGACGGGTTTGAAATGGCTTCGATGTTAGCC
GGGACCCGACTCAGATCGATGCTATAGAAGACAAACAAGGAAAGGTTTTTTTTCC
TTTTGCATC

```
    120 atggctcaatttggaggacagaagaatccgccatgggctactcag
        M  A  Q  F  G  G  Q  K  N  P  P  W  A  T  Q
    165 tttacagccactgcagtatcacagccagctgcactgggtgttcaa
        F  T  A  T  A  V  S  Q  P  A  A  L  G  V  Q
    210 cagccatcactccttggagcatctcctaccatttatacacagcaa
        Q  P  S  L  L  G  A  S  P  T  I  Y  T  Q  Q
    255 actgcattggcagcagcaggccttaccacacaaactccagcaaac
        T  A  L  A  A  A  G  L  T  T  Q  T  P  A  N
    300 tatcagttaacacaaactgctgcattgcagcaacaagccgcagct
        Y  Q  L  T  Q  T  A  A  L  Q  Q  Q  A  A  A
    345 gcagcagctgcattacaacagcaatattcacaacctcagcaggcc
        A  A  A  A  L  Q  Q  Q  Y  S  Q  P  Q  Q  A
    390 ctgtatagtgtgcaacaacagttacagcaaccccagcaaaccctc
        L  Y  S  V  Q  Q  Q  L  Q  Q  P  Q  Q  T  L
    435 ttaacacagccagctgttgcactgcctacaagccttagcctgtct
        L  T  Q  P  A  V  A  L  P  T  S  L  S  L  S
    480 actcctcagccaacagcacaaataactgtatcatatccaacacca
        T  P  Q  P  T  A  Q  I  T  V  S  Y  P  T  P
    525 aggtccagtcaacagcaaacccagcctcagaagcagcgtgttttc
        R  S  S  Q  Q  Q  T  Q  P  Q  K  Q  R  V  F
    570 acaggggtggttacaaaactacatgatacatttggatttgtggat
        T  G  V  V  T  K  L  H  D  T  F  G  F  V  D
    615 gaagatgtattctttcagcttagtgctgtcaaagggaaaaccccc
        E  D  V  F  F  Q  L  S  A  V  K  G  K  T  P
    660 caagtaggtgacagagtattggttgaagctacttataatcctaat
        Q  V  G  D  R  V  L  V  E  A  T  Y  N  P  N
    705 atgccttttaaatggaatgcacagagaattcaaacactaccaaat
        M  P  F  K  W  N  A  Q  R  I  Q  T  L  P  N
    750 cagaatcagtcgcaaacccagccattactgaagactcctcctgct
        Q  N  Q  S  Q  T  Q  P  L  L  K  T  P  P  A
    795 gtacttcagccaattgcaccacagacaacatttggtgttcagact
        V  L  Q  P  I  A  P  Q  T  T  F  G  V  Q  T
    840 cagccccagccccagtcactgctgcaggcacagatttcagcagct
        Q  P  Q  P  Q  S  L  L  Q  A  Q  I  S  A  A
    885 tctattacaccactattgcagactcaaccacagcccttattacag
        S  I  T  P  L  L  Q  T  Q  P  Q  P  L  L  Q
```

FIG. 27B

930 cagcctcagcaaaaagctggtttattgcagcctcctgttcgtata
Q P Q Q K A G L L Q P P V R I
975 gtttcacagccacaaccggcacgacgattagatcccccatcccga
V S Q P Q P A R R L D P P S R
1020 ttttcaggaagaaatgacagaggggatcaagtgcctaacagaaaa
F S G R N D R G D Q V P N R K
1065 gatgatcgaagtcgtgagagagagagagaaagacgtagatcgaga
D D R S R E R E R E R R R S R
1110 gaaagatcacctcagaggaaacgttcccgggaaagatctccacga
E R S P Q R K R S R E R S P R
1155 agagagcgagagcgatcacctcggagagttcgacgtgttgttcca
R E R E R S P R R V R R V V P
1200 cgttacacagttcagttttcaaagttttctttagattgtcccagt
R Y T V Q F S K F S L D C P S
1245 tgtgac**atgatg**gaactaaggcgccgttatcaaaatttgtatata
C D **M** **M** E L R R R Y Q N L Y I
1290 cctagtgacttttttgatgctcaatttacatgggtggatgctttc
P S D F F D A Q F T W V D A F
1335 cctttgtcaagaccatttcagctgggaaattactgcaatttttat
P L S R P F Q L G N Y C N F Y
1380 gta**atg**cacagagaagtagagtccttagaaaaaaat**atg**gccatt
V **M** H R E V E S L E K N **M** A I
1425 cttgatccaccagatgctgaccacttatacagtgcaaaggta**atg**
L D P P D A D H L Y S A K V **M**
1470 ctg**atg**gctagccctagt**atg**gaagatttatatcataagtcatgt
L **M** A S P S **M** E D L Y H K S C
1515 gctcttgctgaggacccacaagaacttcgagatggattccaacat
A L A E D P Q E L R D G F Q H
1560 cctgctagacttgttaagttttagtgggc**atg**aaaggcaaggat
P A R L V K F L V G **M** K G K D
1605 gaagct**atg**gccattggaggccactggtctccttcgttggatgga
E A **M** A I G G H W S P S L D G
1650 ccagacccagaaaaagatccctctgtgttgattaagactgctatt
P D P E K D P S V L I K T A I
1695 cgttgttgtaaggctctgacaggcattgatctaagtgtgtgcaca
R C C K A L T G I D L S V C T
1740 caatggtaccgttttgcagagattcgctaccatcgccctgaggag
Q W Y R F A E I R Y H R P E E
1785 acccacaaggggcgtacagttccagctcatgtggagacagtggtt
T H K G R T V P A H V E T V V
1830 ttatttttcccggatgtttggcattgccttcccacccgctcagag
L F F P D V W H C L P T R S E

FIG. 27C

```
1875 tgggaaaccctctcccgaggatacaagcagcagctggtcgagaag
     W  E  T  L  S  R  G  Y  K  Q  Q  L  V  E  K
1920 cttcagggtgaacgcaaggaggctgatggagaacaggatgaagaa
     L  Q  G  E  R  K  E  A  D  G  E  Q  D  E  E
1965 gagaaggatgatggtgaagctaaagaaatttctacacctacccat
     E  K  D  D  G  E  A  K  E  I  S  T  P  T  H
2010 tggtctaaacttgatccaaagacaatgaaggtaaatgacctccga
     W  S  K  L  D  P  K  T  M  K  V  N  D  L  R
2055 aaagaattagaaggtcgagctcttagttccaaaggattaaaatcc
     K  E  L  E  G  R  A  L  S  S  K  G  L  K  S
2100 cagttaatagcccgattgacaaaacagcttaaagtagaggaacaa
     Q  L  I  A  R  L  T  K  Q  L  K  V  E  E  Q
2145 aaagaagaacagaaggagttagagaaatctgaaaaagaagaggat
     K  E  E  Q  K  E  L  E  K  S  E  K  E  E  D
2190 gaggatgatgataggaaatctgaagacgataaagaggaagaagaa
     E  D  D  D  R  K  S  E  D  D  K  E  E  E  E
2235 aggaaacgtcaagaggaaatagaacgccagcgtcgagaaagaaga
     R  K  R  Q  E  E  I  E  R  Q  R  R  E  R  R
2280 tatattttgcctgatgaaccggccatcattgtacatccaaattgg
     Y  I  L  P  D  E  P  A  I  I  V  H  P  N  W
2325 gctgcaaaaagtggcaagtttgattgtagcatcatgtctttgagt
     A  A  K  S  G  K  F  D  C  S  I  M  S  L  S
2370 gtcctattggactacagattagaggataataaagaacattcattt
     V  L  L  D  Y  R  L  E  D  N  K  E  H  S  F
2415 gaggtttcattgtttgcggaacttttcaacgaaatgcttcaaaga
     E  V  S  L  F  A  E  L  F  N  E  M  L  Q  R
2460 gattttggtgtccgtatatacaaatcattactgtctcttcctgag
     D  F  G  V  R  I  Y  K  S  L  L  S  L  P  E
2505 aaagaggacaaaaaagaaaaggataaaaaaagcaaaaaagatgag
     K  E  D  K  K  E  K  D  K  K  S  K  K  D  E
2550 agaaaagataaaaaagaagaaagagatgatgaaactgatgaacca
     R  K  D  K  K  E  E  R  D  D  E  T  D  E  P
2595 aaacccaaacggagaaaatcaggcgatgataaagataaaaaagaa
     K  P  K  R  R  K  S  G  D  D  K  D  K  K  E
2640 gatagagatgaaaggaagaaagaagataaaagaaaaggtgattct
     D  R  D  E  R  K  K  E  D  K  R  K  G  D  S
2685 aaagatgatgatgaaactgaagaagataacaatcaagatgaatat
     K  D  D  D  E  T  E  E  D  N  N  Q  D  E  Y
2730 gaccctatggaagcagaagaagctgaggatgaagaagatgatagg
     D  P  M  E  A  E  E  A  E  D  E  E  D  D  R
2775 gatgaggaagaaatgaccaaacgagatgacaaaagagatatcaac
     D  E  E  E  M  T  K  R  D  D  K  R  D  I  N
```

FIG. 27D

2820 agatactgcaaggagaggccctctaaagataaggaaaaagaaaag
R Y C K E R P S K D K E K E K
2865 actcaa**atg**atcacaattaacagagatctgtta**atg**gcttttgtt
T Q **M** I T I N R D L L **M** A F V
2910 tattttgatcaaagtcattgtggttaccttcttgaaaaggatttg
Y F D Q S H C G Y L L E K D L
2955 gaagaaatactttatactcttggactacatctttctcgggctcag
E E I L Y T L G L H L S R A Q
3000 gtaaagaagcttcttaataaagtagtgctccgtgaatcttgcttt
V K K L L N K V V L R E S C F
3045 taccggaaattaacagacacctcaaaagatgaagagaaccatgaa
Y R K L T D T S K D E E N H E
3090 gagtctgagtcattgcaggaagat**atg**ctaggaaacagattatta
E S E S L Q E D **M** L G N R L L
3135 cttccaacaccaacagtaaagcaggaatcaaaggatgtggaagaa
L P T P T V K Q E S K D V E E
3180 aatgttggcctcattgtgtacaatggtgca**atg**gtagatgtagga
N V G L I V Y N G A **M** V D V G
3225 agcctcttgcaaaaattggaaaagagcgaaaaagtaagagctgag
S L L Q K L E K S E K V R A E
3270 gtagaacagaagctgcagttactagaagaaaaaacagatgaagat
V E Q K L Q L L E E K T D E D
3315 gaaaaaaccatattaaatttggagaattccaacaaaagcctctct
E K T I L N L E N S N K S L S
3360 ggtgaactcagagaagttaaaaaggaccttagtcagttacaagaa
G E L R E V K K D L S Q L Q E
3405 aacttaaagatttcagaaaac**atg**agtttacaatttgaaaaccaa
N L K I S E N **M** S L Q F E N Q
3450 **atg**aataagacaatcagaaacttatctacggta**atg**gatgaaatc
M N K T I R N L S T V **M** D E I
3495 cacactgttctcaagaaggataatgtaaagaatgaagacaaagat
H T V L K K D N V K N E D K D
3540 caaaaatccaaggagaatggtgccagtgta**tga** 3572
Q K S K E N G A S V *

TAAAATCCATGTAGTGATGAGGAATGGTGTTAAATAATGTAATATATAAAAATCA
TGATATAAGAATGTTTGAAGGTGATGCATGTTTGATTTTAGTAGTATAAATGTAT
TTTAGTTCAAATGATGTATAAAGTTTTATGAATGTGAGTTTCTGCTTTTGAAAAT
TGCTTGTAATTCCTAGCCTTCAAATTATTAAACACTCCTTGAGTGAAATAATTTT
GCATTGCAAAGTGTTTTAGGATGAACTTTGTTATAGTTTTAACTCCAATAAAGTT
CATCAGTTT

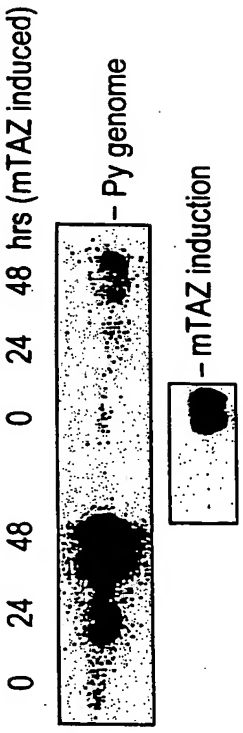
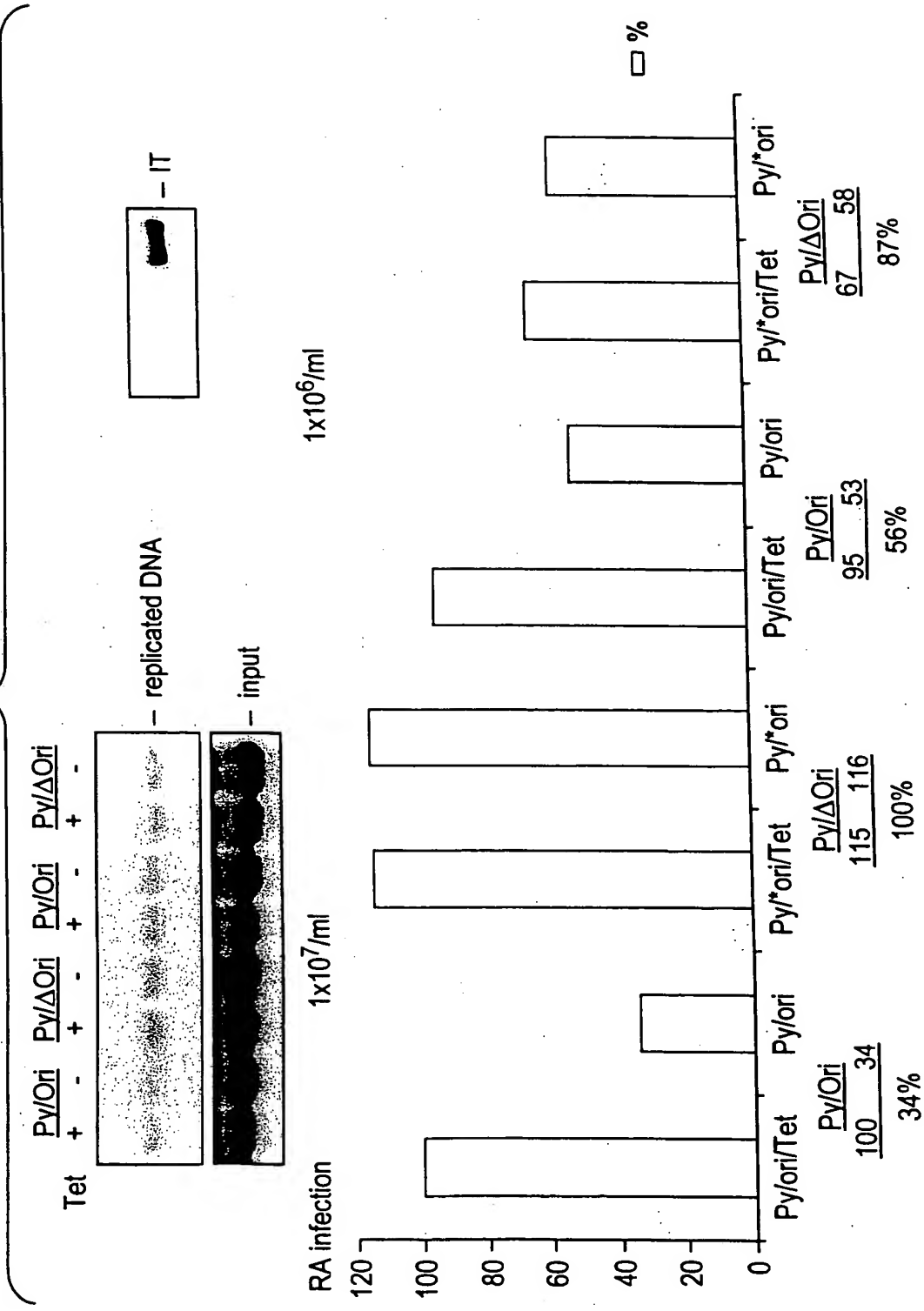


FIG. 28

FIG. 29


Py/Ori Py/ΔOri Py/Ori Py/ΔOri
Tet + - + - + - + -
replicated DNA
input
IT
1x10^6/ml
1x10^7/ml
RA infection
%
120
100
80
60
40
20
0
Py/ori/Tet
Py/ori
Py/*ori/Tet
Py/*ori
Py/ori/Tet
Py/ori
Py/*ori/Tet
Py/*ori
Py/Ori 100 34 34%
Py/ΔOri 115 116 100%
Py/Ori 95 53 56%
Py/ΔOri 67 58 87%

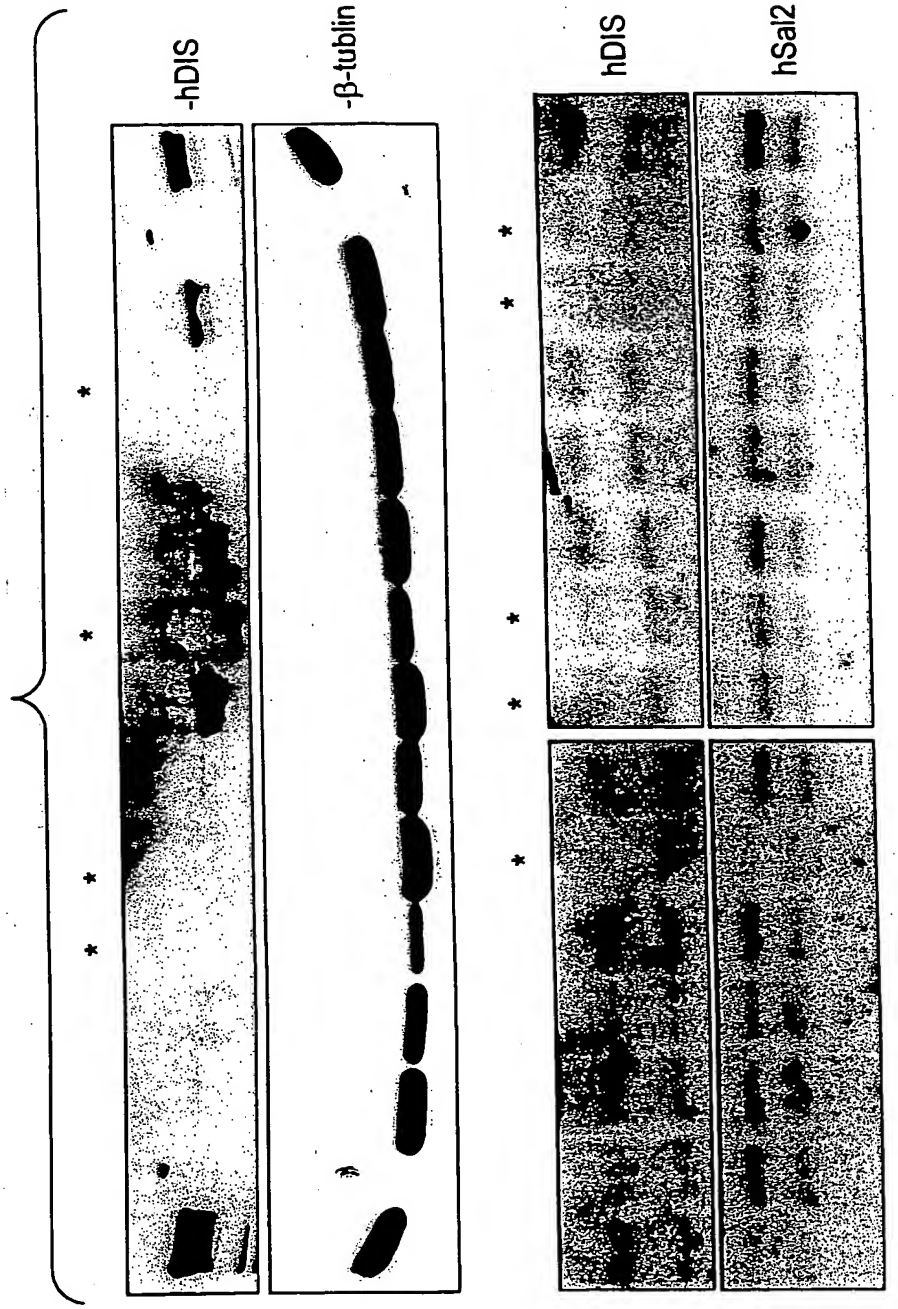


FIG. 30

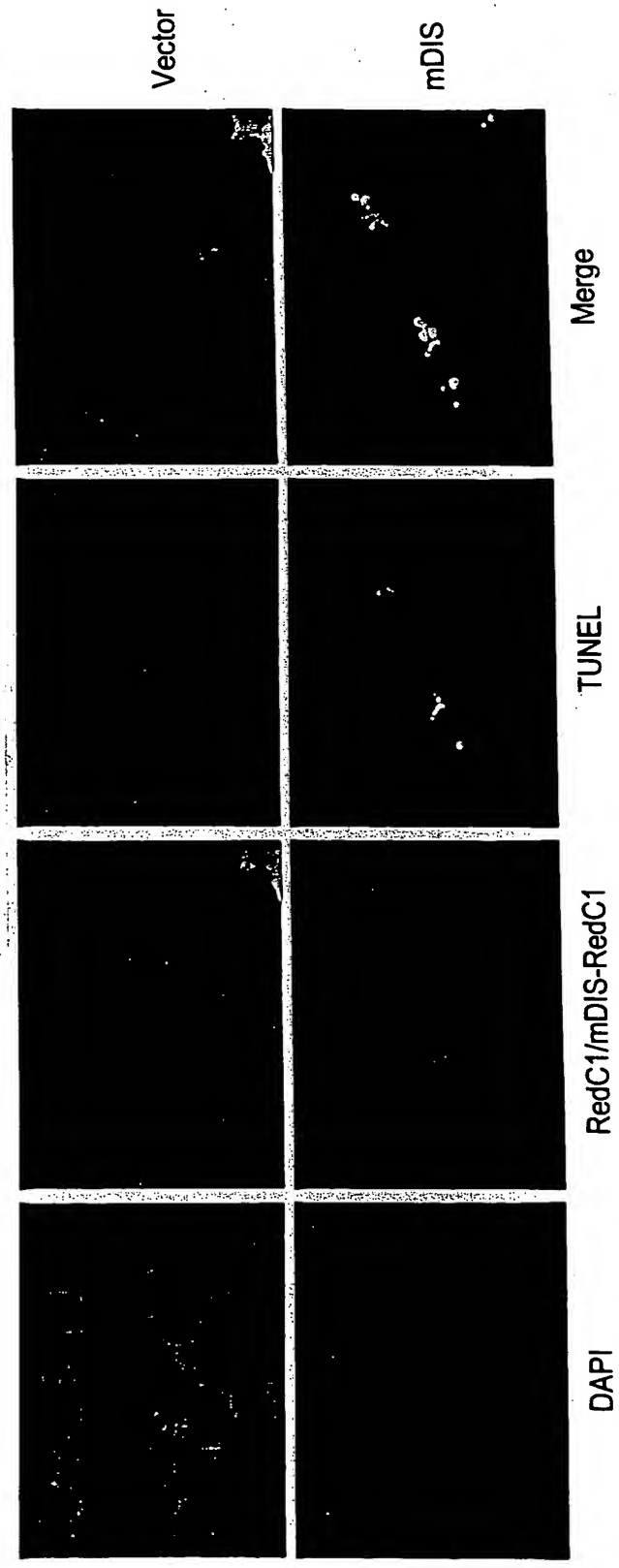


FIG. 31

FIG. 32A

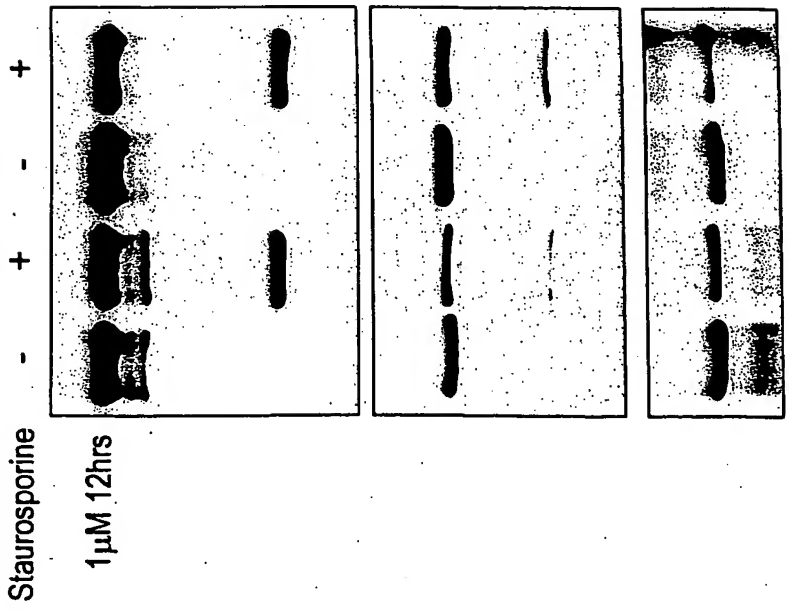


FIG. 32B

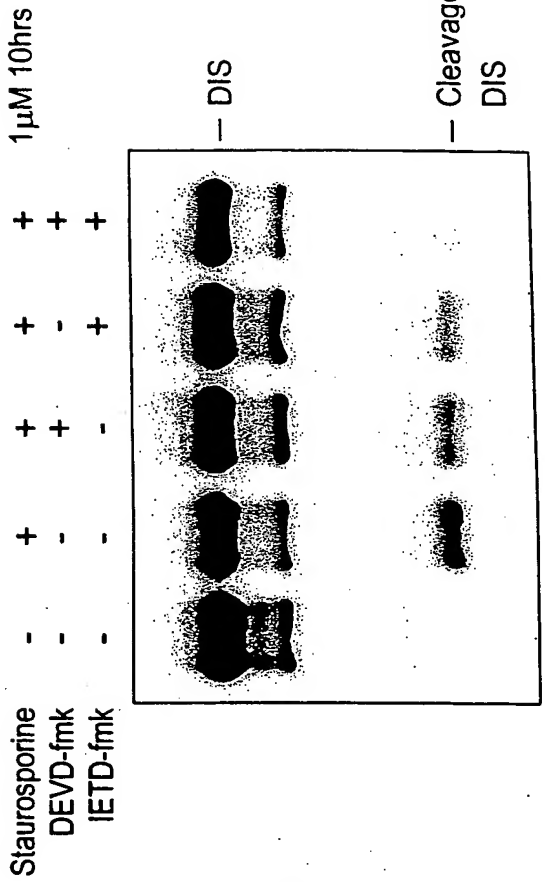


FIG. 33

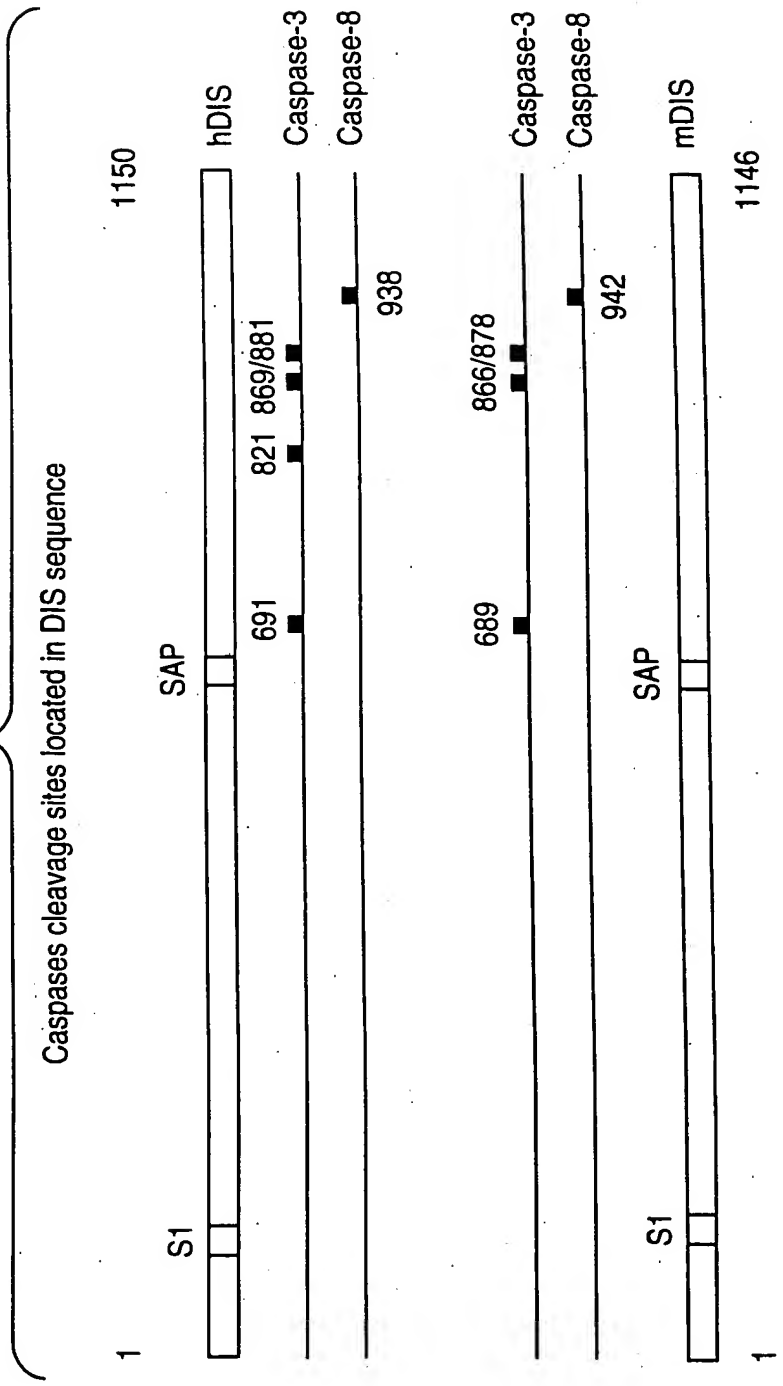

Caspases cleavage sites located in DIS sequence
1
1150
S1
SAP
hDIS
691
821
869/881
Caspase-3
Caspase-8
938
1
1146
S1
SAP
mDIS
689
866/878
Caspase-3
Caspase-8
942

FIG. 34

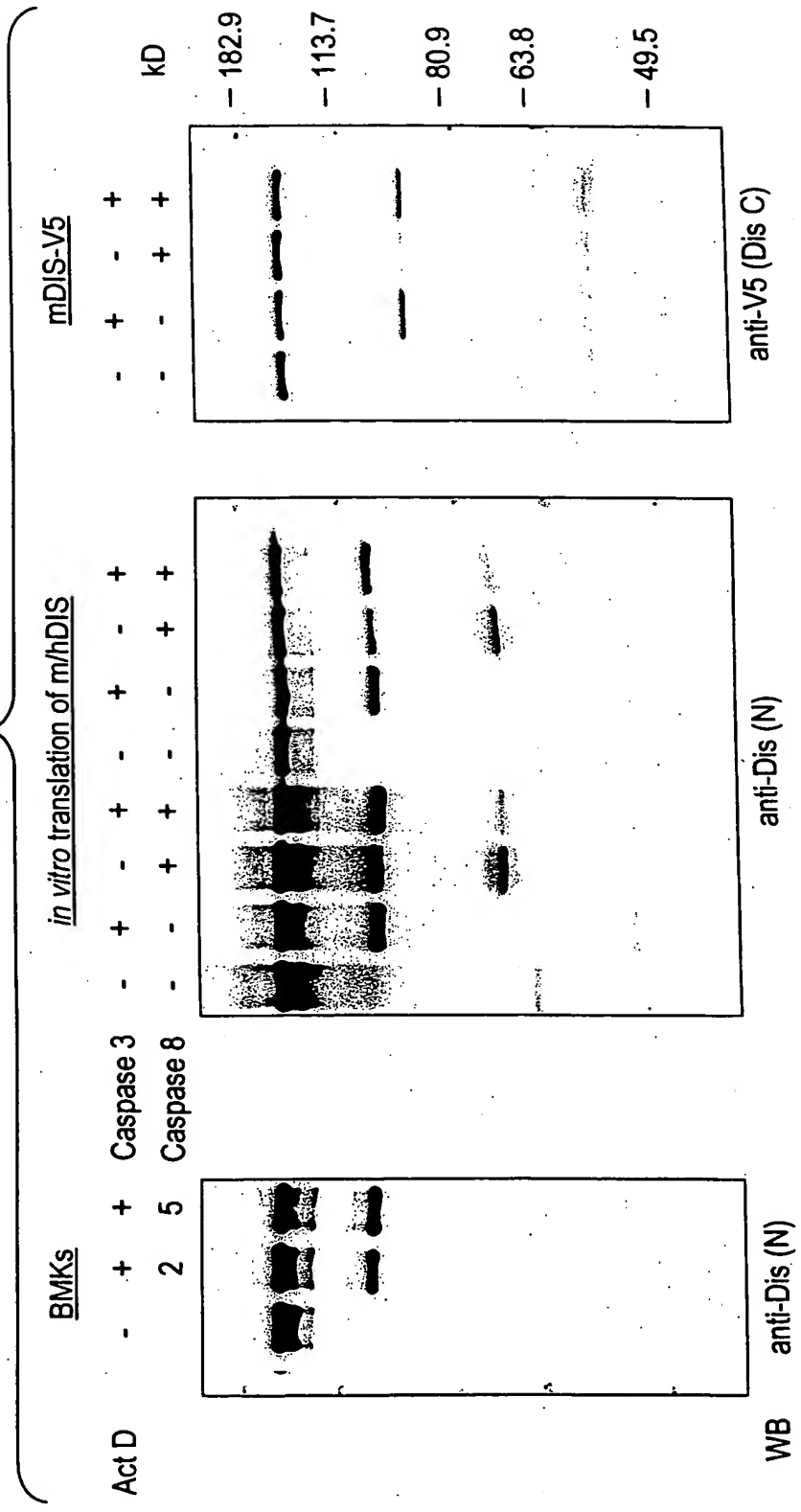
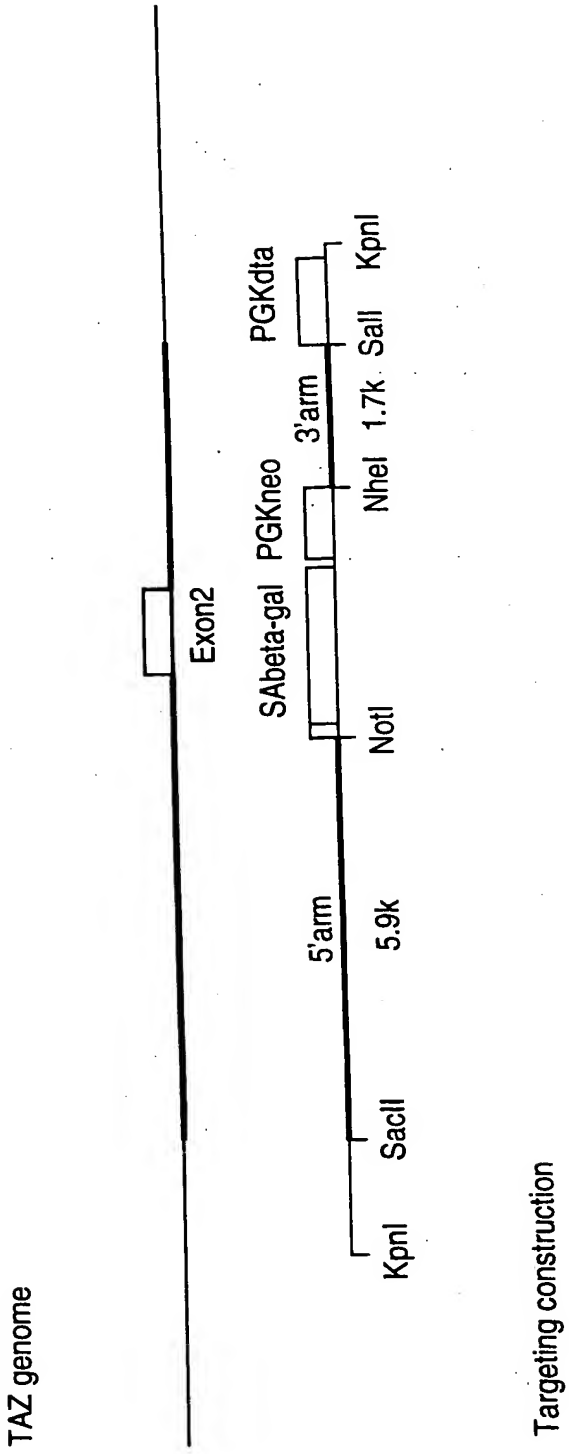

BMKs
in vitro translation of m/hDIS
mDIS-V5
Act D
Caspase 3
Caspase 8
2
5
kD
182.9
113.7
80.9
63.8
49.5
WB
anti-Dis (N)
anti-Dis (N)
anti-V5 (Dis C)

FIG. 35


TAZ genome
Exon2
SAbeta-gal
PGKneo
PGKdta
5'arm
3'arm
5.9k
1.7k
NotI
NheI
SalI
KpnI
SacII
KpnI
Targeting construction

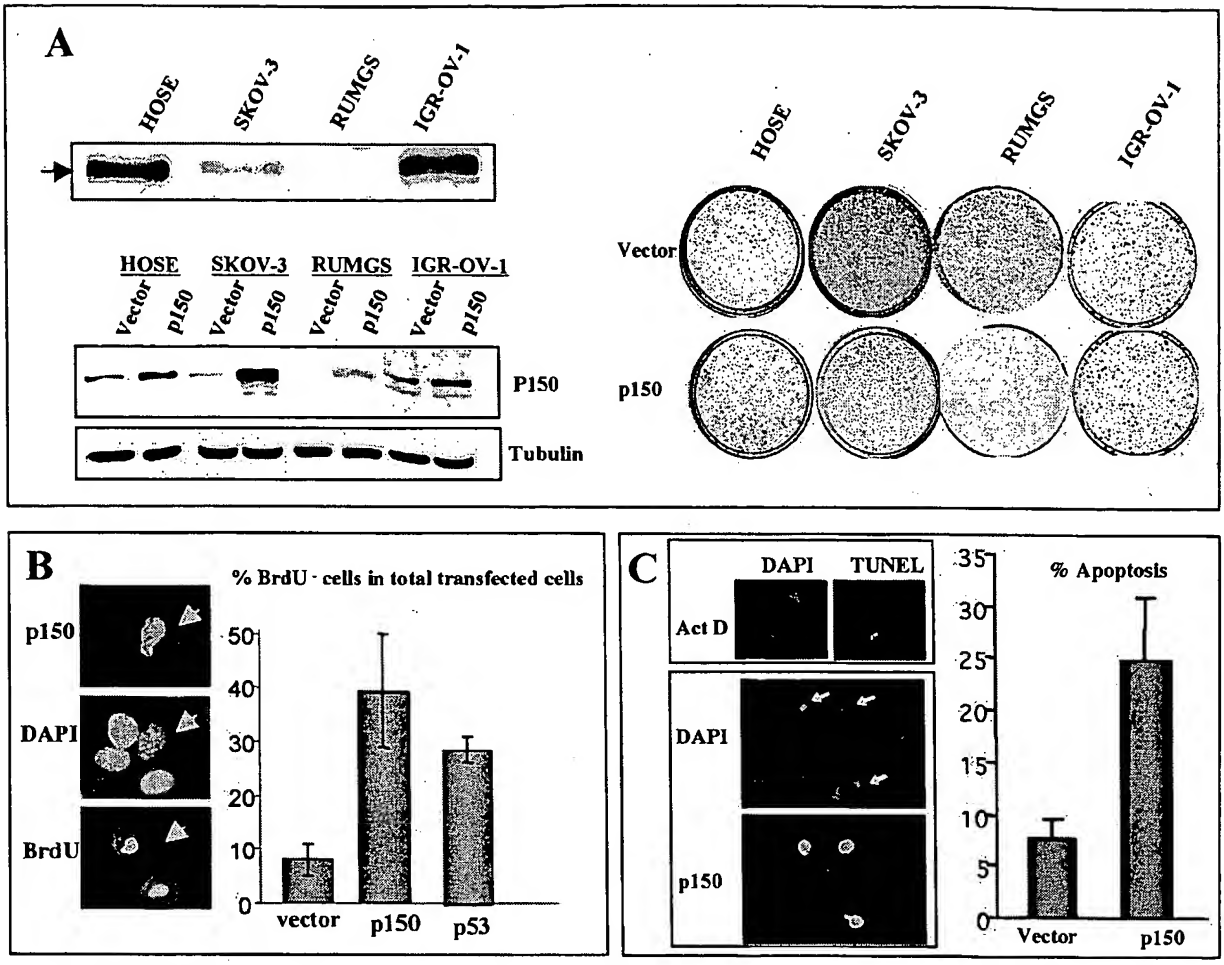

A
HOSE
SKOV-3
RUMGS
IGR-OV-1
HOSE
SKOV-3
RUMGS
IGR-OV-1
Vector
p150
Vector
p150
Vector
p150
Vector
p150
P150
Tubulin
HOSE
SKOV-3
RUMGS
IGR-OV-1
Vector
p150
B
% BrdU - cells in total transfected cells
p150
DAPI
BrdU
50
40
30
20
10
0
vector
p150
p53
C
DAPI
TUNEL
Act D
DAPI
p150
% Apoptosis
35
30
25
20
15
10
5
0
Vector
p150

FIG. 36

FIG. 37

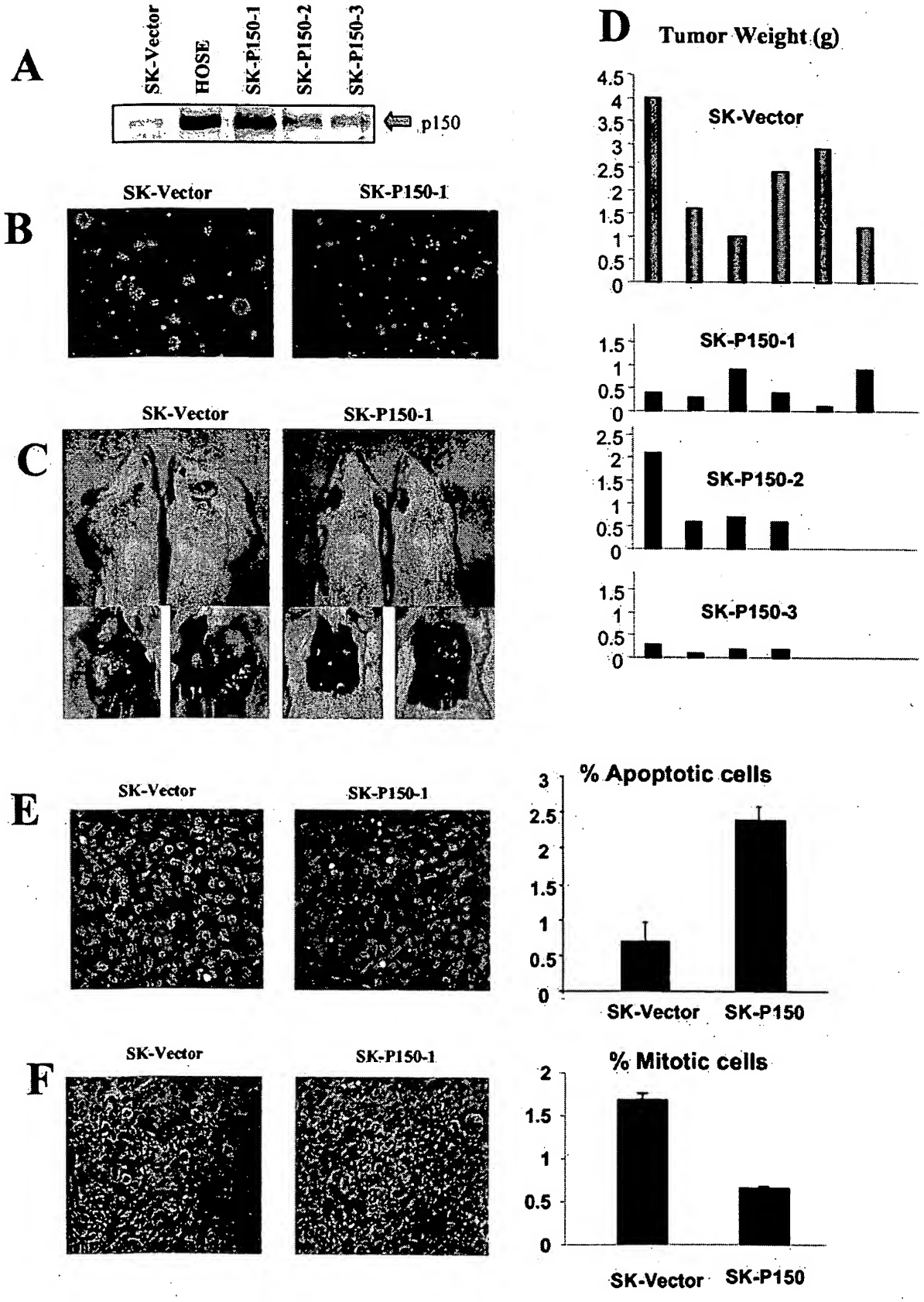

A
SK-Vector
HOSE
SK-P150-1
SK-P150-2
SK-P150-3
p150
B
SK-Vector
SK-P150-1
C
SK-Vector
SK-P150-1
D
Tumor Weight (g)
SK-Vector
SK-P150-1
SK-P150-2
SK-P150-3
E
SK-Vector
SK-P150-1
% Apoptotic cells
SK-Vector
SK-P150
F
SK-Vector
SK-P150-1
% Mitotic cells
SK-Vector
SK-P150

FIG. 38

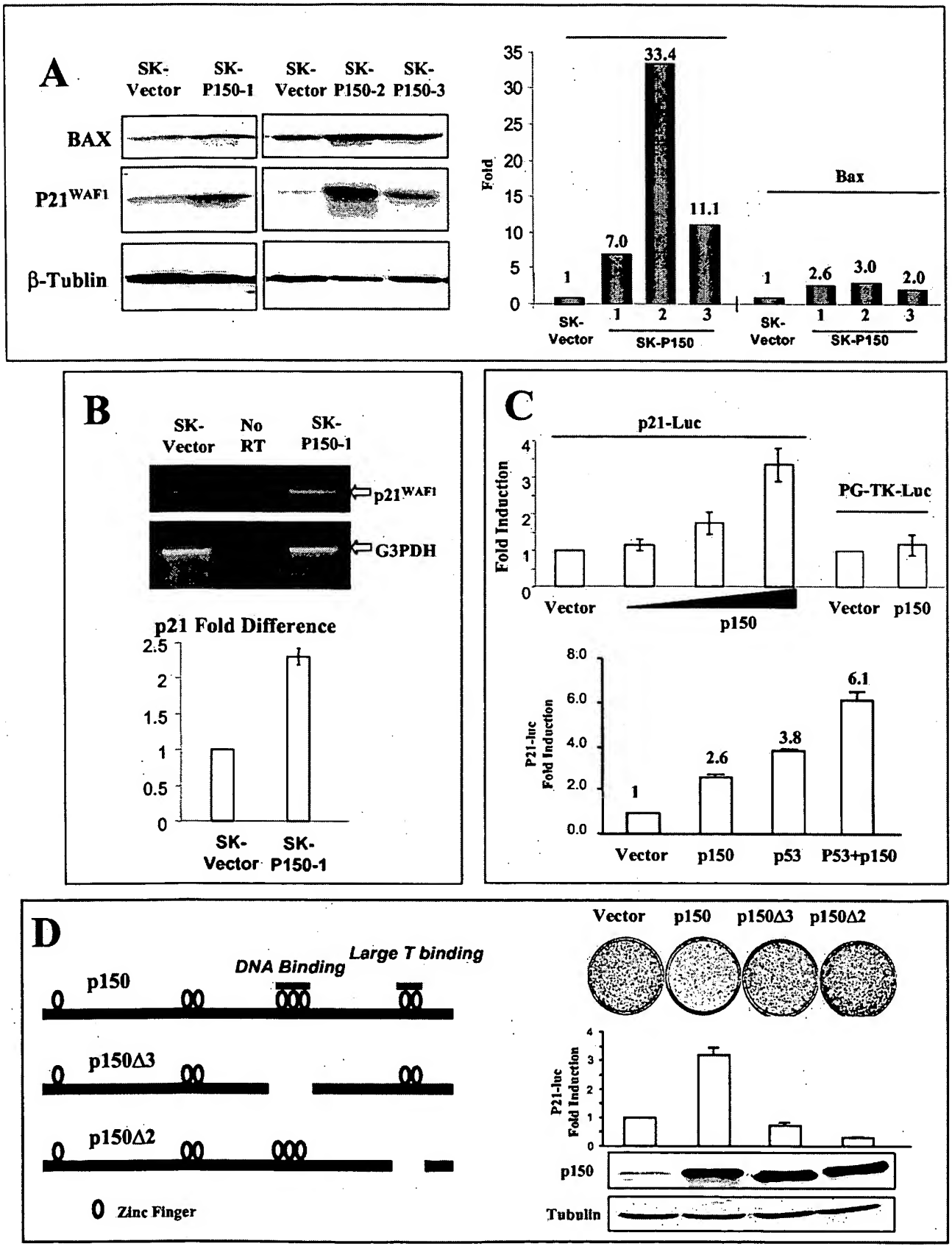
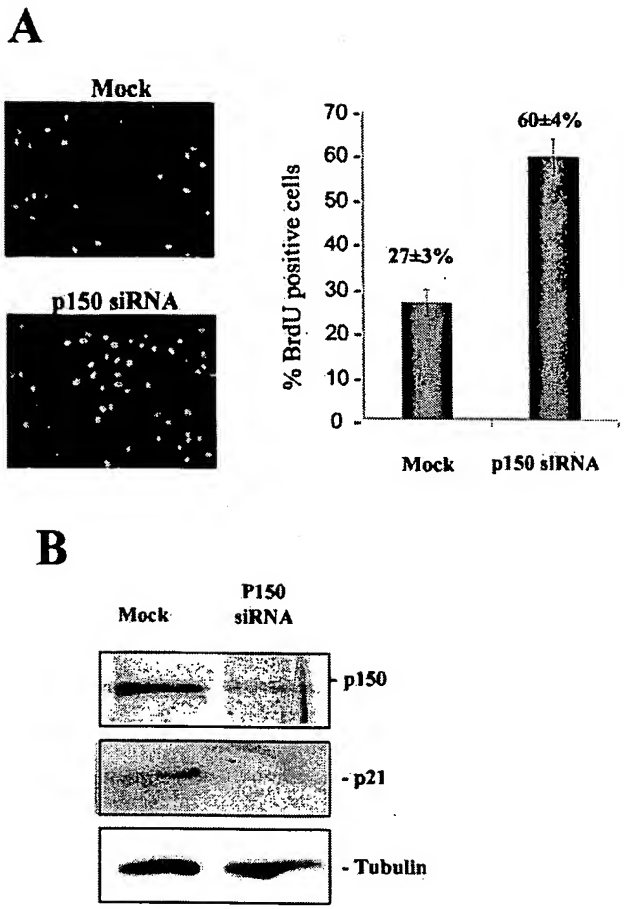

A
SK-Vector
SK-P150-1
SK-Vector
SK-P150-2
SK-P150-3
BAX
P21WAF1
β-Tublin
Fold
Bax
33.4
11.1
7.0
1
2.6
3.0
2.0
SK-Vector
SK-P150
B
SK-Vector
No RT
SK-P150-1
p21WAF1
G3PDH
p21 Fold Difference
C
p21-Luc
PG-TK-Luc
Fold Induction
Vector
p150
P21-luc Fold Induction
6.1
3.8
2.6
p53
P53+p150
D
DNA Binding
Large T binding
p150
p150Δ3
p150Δ2
Zinc Finger
Vector
p150Δ3
p150Δ2
Tubulin

FIG. 39


A
Mock
p150 siRNA
% BrdU positive cells
70
60
50
40
30
20
10
0
27±3%
60±4%
Mock
p150 siRNA
B
Mock
P150 siRNA
p150
p21
Tubulin

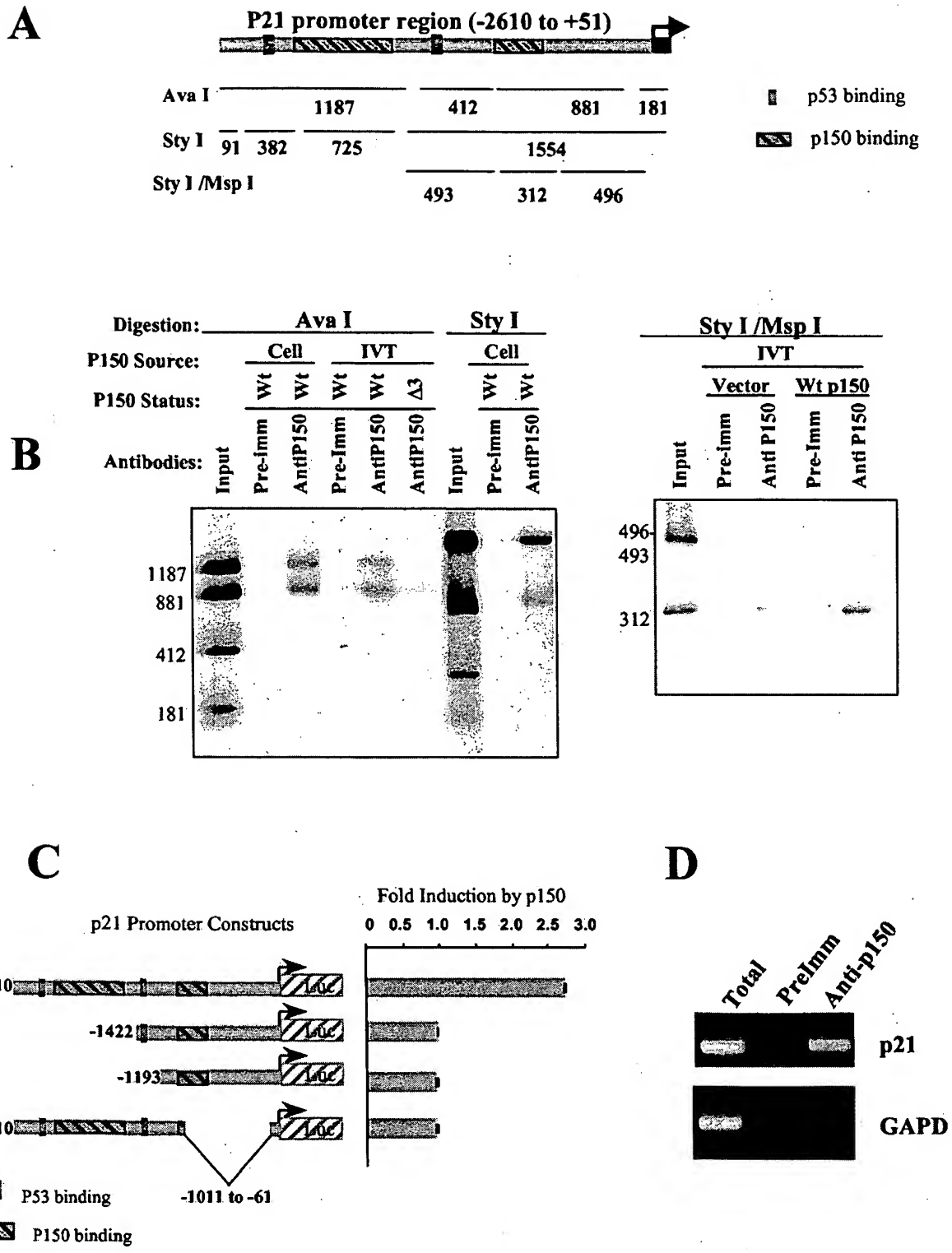

A
P21 promoter region (-2610 to +51)
Ava I
1187
412
881
181
Sty I
91
382
725
1554
Sty I /Msp I
493
312
496
p53 binding
p150 binding
B
Digestion:
Ava I
Sty I
Sty I /Msp I
P150 Source:
Cell
IVT
Cell
IVT
P150 Status:
Wt
Wt
Wt
Wt
Δ3
Wt
Wt
Vector
Wt p150
Antibodies:
Input
Pre-imm
AntiP150
Pre-Imm
AntiP150
AntiP150
Input
Pre-imm
AntiP150
Input
Pre-Imm
Anti P150
Pre-Imm
Anti P150
1187
881
412
181
496
493
312
C
p21 Promoter Constructs
Fold Induction by p150
0 0.5 1.0 1.5 2.0 2.5 3.0
-2610
-1422
-1193
-2610
-1011 to -61
P53 binding
P150 binding
D
Total
PreImm
Anti-p150
p21
GAPD

FIG. 40

Suppression of HPV-16 replication origin replication by hSal2 in C33A cells

HPV116 Ori	+	+	+	+
HPV-16 E1, E2	-	+	+	+
hSal2	-	-	+(1x)	+(2x)
% Replicated DNA	3.37	45.47	33.03	26.23
% Suppressed DNA	92.6	0	26.76	42.16

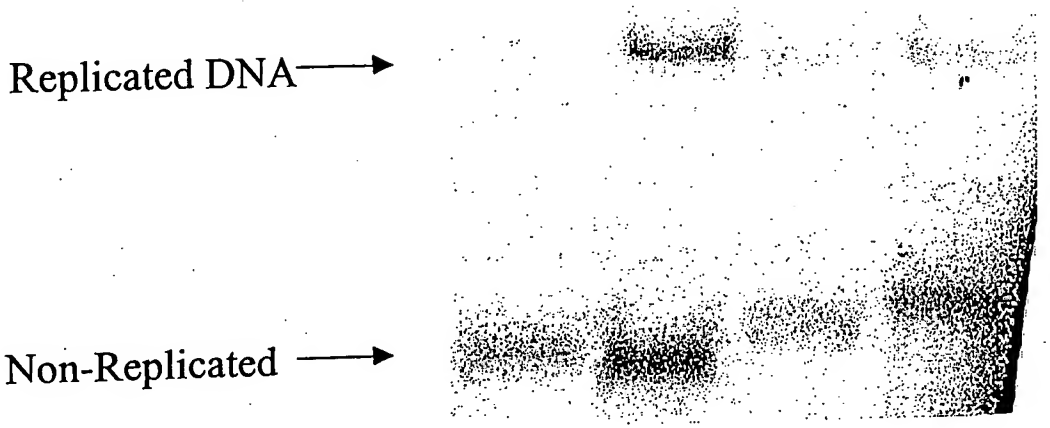


FIG. 41

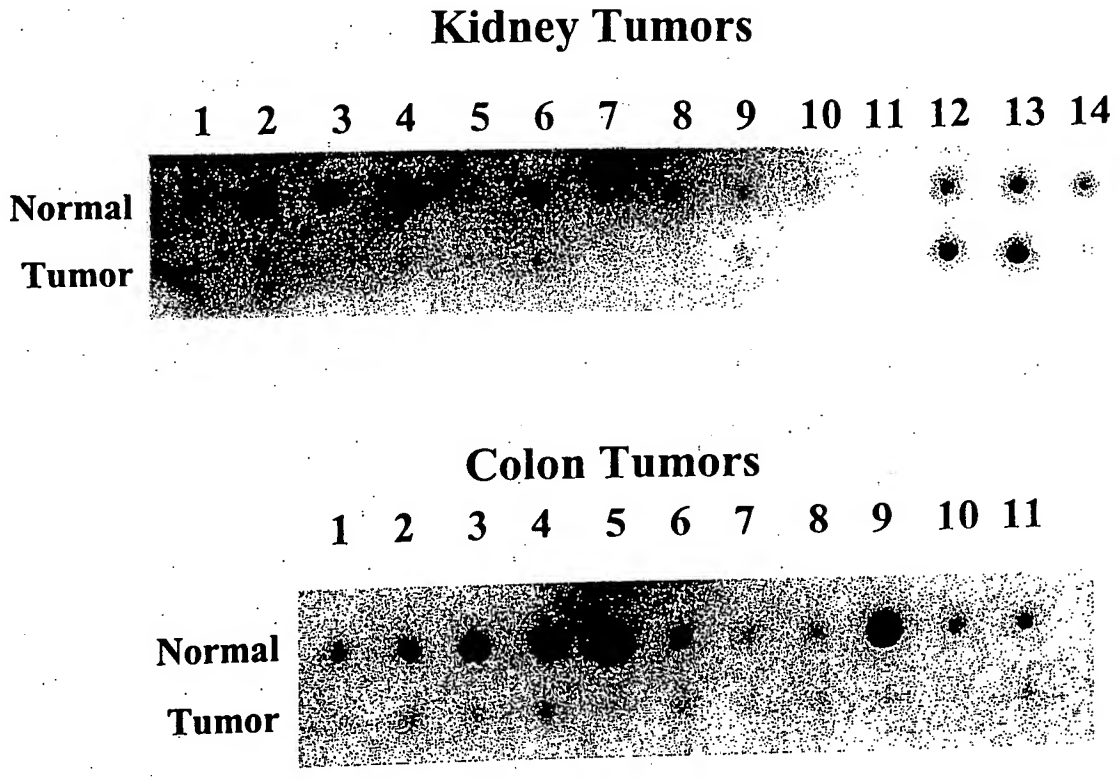

Kidney Tumors
1 2 3 4 5 6 7 8 9 10 11 12 13 14
Normal
Tumor
Colon Tumors
1 2 3 4 5 6 7 8 9 10 11
Normal
Tumor

FIG. 42